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(54) Title: CHK1 KINASE INHIBITORS

(57) Abstract: Novel compounds useful in the inhibition of damage response kinases are provided.

CHK1 KINASE INHIBITORS

FIELD OF THE INVENTION

The present invention relates to damage response kinase inhibitors, especially checkpoint kinase ("chk1 kinase") inhibitors, pharmaceutical compositions comprising these compounds and methods of using these compounds to treat various forms of cancer and hyperproliferative disorders.

BACKGROUND OF THE INVENTION

The cellular response to DNA damage involves cell cycle delays, increased repair and apoptosis (Zhou and Elledge *Nature* 2000. 408:433-439). Although many effective cancer therapies work by causing DNA damage induced apoptosis, resistance to these agents remains a significant limitation in the treatment of cancer. One important mechanism of drug resistance is attributed to cell cycle delays (also called checkpoints) and repair activation, which provides both the opportunity and capacity for cells to repair DNA damage. It is likely that approaches abrogating these survival DNA damage responses would have significant clinical utility.

Among different DNA damage response kinases, Chk1 was linked to survival responses including checkpoints. Mice lacking CHK1 die in early embryogenesis (Liu et al.*Gene & Dev.* 2000 14: 1448-1459; Takai et al, *Gene & Dev.* 2000. 14: 1439-1447). ES cells expressing a conditional CHK1 gene die of p53-independent apoptosis after loss of CHK1. Prior to their death, these cells become incapable of preventing mitotic entry in response to IR (Liu et al.*Gene & Dev.* 2000 14: 1448-1459), demonstrating that Chk1 is required for the G2 DNA damage checkpoint in mammals as previously observed in other organisms.

Chk1 prevents mitotic entry as follows. Arrest in G2 is regulated by the maintenance of inhibitory phosphorylation of Cdc2 (Nurse *Cell* 1997. 91: 865-867). Cdc2 dephosphorylation and activation is catalyzed by the dual specificity phosphatase Cdc25 (Morgan *Nature* 1995. 374: 131-134). Recent evidence indicates that part of the G2/M DNA checkpoint mechanism involves inactivation and translocation of Cdc25C into the cytoplasm. This is at least partially mediated by phosphorylation on Ser-216 in Cdc25C and its consequent binding with 14-3-3

proteins (Peng et al., *Science* 1997. 277: 1501-1505; Dalal et al. *Mol. Cell Bio.* 1999. 19: 4465-4479; Yang et al *EMBO J.* 1999. 18: 2174-2183). Chk1 (Sanchez et al. *Science* 1997. 277: 1497-1501) has been shown to phosphorylate Cdc25C at Ser-216 *in vitro*. This modification is thought to maintain Cdc25C phosphorylation in cells arrested at G2/M in response to DNA damage. Recently, staurosporine-like kinase inhibitors, UCN-01 and SB-218078, have been shown to be potent Chk1 inhibitors (Jackson et al. *Cancer Res.* 2000. 60: 566-572; Graves et al. *J. Biol. Chem.* 2000. 275: 5600-5605). *In vivo*, they can abrogate the G2/M checkpoint induced by DNA damaging agents and enhance the cytotoxicities of the DNA damaging agents. Thus it is likely that a specific Chk1 inhibitor could be used clinically in combination treatment with coventional therapies. Since Chk1 is an essential kinase for regular cell cycle (Liu et al.*Gene & Dev.* 2000 14: 1448-1459), it is possible that Chk1 inhibitor could also be used alone in cancer therapy.

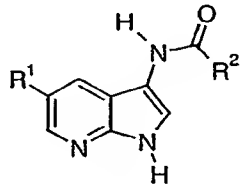
Based on the foregoing, there is a need to identify a potent chk1 kinase inhibitors for the treatment of the various aforementioned indications.

SUMMARY OF THE INVENTION

The present invention involves pyrolo[2,3-*b*]pyridine compounds represented by Formula (I) hereinbelow, pharmaceutical compositions comprising such compounds and methods of inhibiting kinase as well as specific assays to detect inhibition of chk1 kinase activity.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides compounds of Formula (I), hereinbelow:



(I)

wherein:

R^1 is aryl or heteroaryl, wherein aryl or heteroaryl may optionally be substituted by one or more of group A and on any position with the exception that R^1 is not 3,4-dichlorophenyl, with the preferred substitution being 3-,4- or 5-alkoxy- or hydroxy-

or amino- or hydroxymethyl- or aminomethyl- or acetamido- or aminosulfamoyl- or dimethylamino- phenyl including di- and tri-substitution or 3-thienyl, with the more preferred substitution being 4-hydroxy-3-methoxyphenyl or 3-acetamidophenyl or 3,4-dimethoxyphenyl or 4-aminophenyl or 4-aminomethylphenyl or 4-dimethylaminomethylphenyl;

A is selected from the group consisting of C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, C_{0-6} alkylheteroaryl, $C(=NH)R^3$, COR^3, $CONR^3R^4$, $CON(O)R^3R^4$, CO_2R^3, $C(O)SR^3$, $C(S)R^3$, cyano, trifluoromethyl, NR^3R^4, $N(O)R^3R^4$, NR^3COR^4, $NR^3CONR^4R^5$, $NR^3CON(O)R^4R^5$, $NR^3CO_2R^3$, $NR^3C(O)SR^3$, $NR^3SO_2R^3$, nitro, OR^3, OCF_3, aryloxy, heteroaryloxy, SR^3, $S(O)R^3$, $S(O)_2R^3$, SCF_3, $S(O)CF_3$, $S(O)_2CF_3$, $SO_2NR^3R^4$, SO_3R^3, $PO_3R^3R^4$, and halo, wherein C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-5} alkylaryl, C_{0-5} alkylheterocyclyl, C_{0-5} alkylheteroaryl, $(CH_2)_{0-5}$heteroaryl, aryloxy, and heteroaryloxy may be optionally substituted by one or more of group B and on any position;

B is selected from the group consisting of C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-5} alkylaryl, C_{0-5} alkylheterocyclyl, C_{0-6} alkylheteroaryl, $C(=NH)R^3$, COR^3, $CONR^3R^4$, $CON(O)R^3R^4$, CO_2R^3, $C(O)SR^3$, $C(S)R^3$, cyano, trifluoromethyl, NR^3R^4, $N(O)R^3R^4$, NR^3COR^4, $NR^3CONR^4R^5$, $NR^3CON(O)R^4R^5$, $NR^3CO_2R^3$, $NR^3C(O)SR^3$, $NR^2SO_2R^3$, nitro, OR^3, OCF_3, aryloxy, heteroaryloxy, SR^3, $S(O)R^3$, $S(O)_2R^3$, SCF_3, $S(O)CF_3$, $S(O)_2CF_3$, $SO_2NR^3R^4$, SO_3R^3, $PO_3R^3R^4$, and halo, wherein C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, C_{0-6} alkylheteroaryl, $(CH_2)_{0-6}$heteroaryl, aryloxy, and heteroaryloxy may be optionally substituted by one or more of group C and on any position;

R^3, R^4, and R^5 are independently selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, and C_{0-6} alkylheteroaryl; or R^3 and R^4 taken together with the nitrogen to which they are attached form a ring having 3 to 7 carbon atoms optionally containing 1, 2, or 3 heteroatoms selected from nitrogen, sulfur, oxygen, or nitrogen, substituted with hydrogen, C_{1-6} alkyl or $(CH_2)_{0-3}$aryl, wherein any of the

foregoing may be optionally substituted by one or more of group C and on any position;

C is selected from the group consisting of C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, C_{0-6} alkylheteroaryl, $C(=NH)R^6$, COR^6, $CONR^6R^7$, $CON(O)R^6R^7$, CO_2R^6, $C(O)SR^6$, $C(S)R^6$, cyano, trifluoromethyl, NR^6R^7, $N(O)R^6R^7$, NR^6COR^6, $NR^6CONR^7R^8$, $NR^6CON(O)R^7R^8$, $NR^6CO_2R^6$, $NR^6C(O)SR^6$, $NR^6SO_2R^6$, nitro, OR^6, OCF_3, aryloxy, heteroaryloxy, SR^6, $S(O)R^6$, $S(O)_2R^6$, SCF_3, $S(O)CF_3$, $S(O)_2CF_3$, $SO_2NR^6R^7$, SO_3R^6, $PO_3R^6R^7$, and halo, wherein C_{1-8} alkyl, C_{1-8} alkanoyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, C_{0-6} alkylheteroaryl may be optionally substituted by one or more of $C(=NH)R^6$, COR^6, $CONR^6R^7$, $CON(O)R^6R^7$, CO_2R^6, $C(O)SR^6$, $C(S)R^6$, cyano, trifluoromethyl, NR^6R^7, $N(O)R^6R^7$, NR^6COR^6, $NR^6CONR^7R^8$, $NR^6CON(O)R^7R^8$, $NR^6CONR^6R^7R^8Y$, $NR^6CO_2R^6$, $NR^6C(O)SR^6$, $NR^6SO_2R^6$, nitro, OR^6, aryloxy, heteroaryloxy, SR^6, $S(O)R^6$, $S(O)_2R^6$, $SO_2NR^6R^7$, SO_3R^6, $PO_3R^6R^7$, or halo, and on any position;

R^6, R^7, and R^8 are independently selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, and C_{0-6} alkylheteroaryl; or R^7 and R^8 taken together with the nitrogen to which they are attached form a ring having 3 to 7 carbon atoms optionally containing 1, 2, or 3 heteroatoms selected from nitrogen, sulfur, oxygen, or nitrogen, substituted with hydrogen, C_{1-6} alkyl or $(CH_2)_{0-3}$aryl;

R^2 is selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, C_{3-6} cycloalkyl, OR^9, $NR^{10}R^{11}$, phenyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazolinyl, thiazinyl, pyrrolyl, furyl, thienyl, pyrazolyl, imidazolyl, triazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl and thiadiazolyl, wherein alkyl and alkenyl and cycloalkyl may optionally be substituted with one of more of group D and at any position and wherein phenyl may be optionally subtituted at positions 3-, 4-, and 5- with one to three of group E and wherein pyridyl, pyridazinyl, pyrimidinyl, pyrazolinyl, thiazinyl, pyrrolyl, furyl, thienyl, pyrazolyl, imidazolyl, triazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl and thiadiazolyl may optionally be substituted by one or more of group F and at any position, with the preferred substitution being *n*-

propyl or pyridyl or pyrazolinyl, with the more preferred substitution being 3-pyridyl.

R^9 is hydrogen or C_{1-6} alkyl, wherein any of the foregoing groups are optionally substituted with one or more of group D and at any position, with the exception that R^9 is not *tert*-butyl;

R^{10} is selected from the group consisting of hydrogen, methyl and ethyl;

R^{11} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-8} alkenyl and C_{3-6} cycloalkyl, wherein any of the foregoing groups are optionally substituted with one or more of group D and at any position;

R^{10} and R^{11} taken together with the nitrogen to which they are attached may form a ring having 3 to 7 carbon atoms optionally containing 1, 2, or 3 heteroatoms selected from nitrogen, sulfur, oxygen, or nitrogen, substituted with hydrogen or C_{1-6} alkyl;

D is selected from the group consisting of C_{1-6} alkyl, C_{2-8} alkenyl, C_{3-6} cycloalkyl, OR^{12}, $OC(O)NR^{12}R^{13}$, $NR^{14}SO_2R^{12}R^{13}$, $NR^{14}C(O)OR^{12}$, $NR^{14}C(O)NR^{12}R^{13}$, halo, cyano, trifluoromethyl, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, SO_3R^{12}, $SO_2NR^{12}R^{13}$, $C(O)SR^{12}$, $CONR^{12}R^{13}$ and PO_3R^{12};

R^{12}, R^{13}, R^{14} are independently selected from the group consisting of hydrogen, C_{1-3} alkyl, C_{2-3} alkanoyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and C_{3-5} cycloalkyl; or R^{12} and R^{13} taken together with the nitrogen to which they are attached form a ring having 3 to 7 carbon atoms optionally containing 1, 2, or 3 heteroatoms selected from nitrogen, sulfur, oxygen, or nitrogen, substituted with hydrogen or C_{1-3} alkyl;

E is selected from the group consisting of C_{1-4} alkyl, OR^{15} and $NR^{15}R^{16}$, with the exception that R^2 is not 3,4-dimethoxyphenyl or 3-methoxyphenyl,

F is selected from the group consisting of C_{1-6} alkyl, C_{2-8} alkenyl, C_{3-6} cycloalkyl, OR^{12}, $OC(O)NR^{12}R^{13}$, $NR^{12}R^{13}$, $NR^{14}SO_2R^{12}R^{13}$, $NR^{14}C(O)OR^{12}$, $NR^{14}C(O)NR^{12}R^{13}$, halo, cyano, trifluoromethyl, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, SO_3R^{12}, $SO_2NR^{12}R^{13}$, $C(O)SR^{12}$, $CONR^{12}R^{13}$ and PO_3R^{12};

R^{15} and R^{16} are independently selected from the group consisting of hydrogen, C_{1-3} alkyl, C_{2-3} alkanoyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and C_{3-5} cycloalkyl; or R^{15} and R^{16} taken together with the nitrogen to which they are attached form a ring having 3 to 7

carbon atoms optionally containing 1, 2, or 3 heteroatoms selected from nitrogen, sulfur, oxygen, or nitrogen, substituted with hydrogen or C_{1-3} alkyl.

As used herein, the term "alkanoyl " is used herein at all occurrences to mean a C(O)alkyl group, wherein the alkyl portion is as defined below, including, but not limited to, acetyl, pivaloyl, and the like.

The term "alkenyl" is used herein at all occurrences to mean a straight or branched chain radical, wherein there is at least one double bond between two of the carbon atoms in the chain, including, but not limited to, ethenyl, 1-propenyl, 2-propenyl, 2-methyl-1-propenyl, 1-butenyl, 2-butenyl, and the like.

The term "alkoxy" is used herein at all occurrences to mean a straight or branched chain radical bonded to an oxygen atom, including, but not limited to, methoxy, ethoxy, n- propoxy, isopropoxy, and the like.

The term "alkyl" refers to a saturated hydrocarbon group joined together by single carbon-carbon bonds. The alkyl hydrocarbon group may be linear, or branched, including, but not limited to methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, and the like.

The term "alkylaryl" is used herein at all occurrences to mean a aryl group as defined below attached to an alkyl group as defined above, including, but not limited to, benzyl and phenethyl, and the like.

The term "alkylheterocyclyl" is used herein at all occurrences to mean a heterocyclic group as defined below attached to an alkyl group as defined above, including, but not limited to, (tetrahydro-3-furanyl)methyl and 3-(4-morpholinyl)propyl, and the like.

The term "alkylheteroaryl" is used herein at all occurrences to mean a heteroaryl group as defined below attached to an alkyl group as defined above, including, but not limited to, 3-(furanyl)methyl and (2-pyridinyl)propyl, and the like.

The term "alkynyl" is used herein at all occurrences to mean a straight or branched chain radical, wherein there is at least one triple bond between two of the carbon atoms in the chain, including, but not limited to, acetylene, 1- propylene, 2-propylene, and the like.

The term "aryl" is used herein at all occurrences to mean 6-14-membered substituted or unsubstituted aromatic ring(s) or ring systems which may include bi- or tri-cyclic systems, including, but not limited to phenyl, naphthalenyl, biphenyl, phenanthryl, anthracenyl, and the like.

The term "aryloxy" is used herein at all occurrences to mean an aryl group as defined above linked via an oxy group, including, but not limited to, phenoxy, and the like.

The terms "cycloalkyl" is used herein at all occurrences to mean cyclic radicals, which may be mono- or bicyclo- fused ring systems which may additionally include unsaturation, including, but not limited to, cyclopropyl, cyclopentyl, cyclohexyl, 1,2,3,4-tetrahydronaphthalenyl, and the like.

The terms "halo" or "halogen" are used interchangeably herein at all occurrences to mean radicals derived from the elements chlorine, fluorine, iodine and bromine.

The term "heteroaryl" is used herein at all occurrences to mean a 5-14-membered substituted or unsubstituted aromatic ring(s) or ring systems which may include bi- or tri-cyclic systems, which ring or ring systems contain 1 to 4 heteroatoms selected from nitrogen, which may be optionally substituted with hydrogen or C_{1-8}alkyl, oxygen, and sulfur, including, but not limited to, indolyl, benzofuranyl, thianaphthenyl, quinolyl, isoquinolyl, pyrrolyl, furanyl, thienyl, pyridyl, and the like.

The term "heteroaryloxy" is used herein at all occurrences to mean an heteroaryl group as defined above linked via an oxy group, including, but not limited to, 2-pyridinyloxy, and the like.

The term "heterocyclic" is used herein at all occurrences to mean a saturated or wholly or partially unsaturated 5-10-membered ring system (unless the cyclic ring system is otherwise limited) in which one or more rings contain one or more heteroatoms selected from nitrogen, which may be optionally substituted with hydrogen or C_{1-8}alkyl, oxygen, and sulfur, including, but not limited to, pyrrolidine, piperidine, piperazine, morpholine, imidazolidine, pyrazolidine, 1,2,3,6-tetrahydropyridine, hexahydroazepine, and the like.

Compounds useful in the present invention include:

3-dimethylamino-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

4-methoxy-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

1-ethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-urea;

benzo[1,3]dioxole-5-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

N-(5-(3-carboxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-chloro-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

N-(5-(4-carboxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

4-acetylamino-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

N-(5-(3-chloro-phenyl)-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-isonicotinamide;

acetic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-ylcarbamoyl)-methyl ester;

6-(2-(pyrrolidin-1-yl)ethyl-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

3-hydroxy-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

N-(5-(4-cyano-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-acetyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(pyridin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-fluoro-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-methyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-carbamic acid ethyl ester;

N-(5-(4-methylsulfonyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

2-methoxy-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-acetamide;

(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-hydroxymethyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

pyridine-2-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

N-(5-(pyridin-4-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-isobutyramide;

N-(5-(4-dimethylamino-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-hydroxymethyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

6-methyl-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

thiophene-2-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

N-(5-(4-sulfamoylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-aminophenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-acetamido-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-hydroxy -phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

furan-2-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

furan-3-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

thiophene-3-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

pyrrole-2-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

N-(5-(4-methyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-(morpholin-1-yl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-(4-methyl-piperazin-1-yl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

5-methyl-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

5-bromo-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

2,6-dimethoxy-*N*-(5-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-aminomethylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-aminomethylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-(4-t-butoxycarbonyl)-piperazinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-(4-t-butoxycarbonyl)-piperazinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-(4-t-butoxycarbonyl)-methyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-(4-methylpiperazinomethyl)-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-(4-methylpiperazinomethyl)-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

2-methyl-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

2-chloro-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

N-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-2-methoxybenzamide;

2-hydroxy-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

pyrimidine-5-carboxylic acid-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

N-((5-(benzothiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-((5-(thiophen-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-((5-(3-biphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-((5-(benzofuran-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-((5-(indol-5-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide; and

pyrazine-2-carboxylic acid ((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

Preferred compounds useful in the present invention include:

N-(5-(thiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3,4-dimethoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-sulfamoylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-acetamide-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(naphthalen-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

4-methyl-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

pyrazine-2-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

N-(5-(4-aminomethylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-methoxyphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-dimethylamino-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3,4-(methylenedioxy)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-diethanolaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-dimethylaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-(4-methylpiperazinomethyl)-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-diethanolaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3,5-dimethyl-4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-hydroxymethyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

More Preferred compounds useful in the present invention include:

N-(5-(4-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-piperidinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-pyrrolidinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-methylaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(thiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-aminophenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3,4-dimethoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-acetamido-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

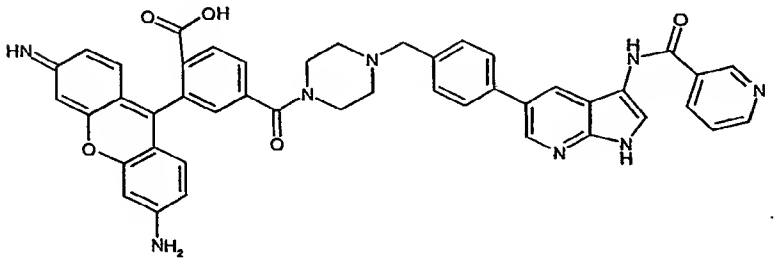
N-(5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-(dimethylaminomethyl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-(morpholin-1-yl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-(4-methyl-piperazin-1-yl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide.

Other compounds useful in the present invention include:



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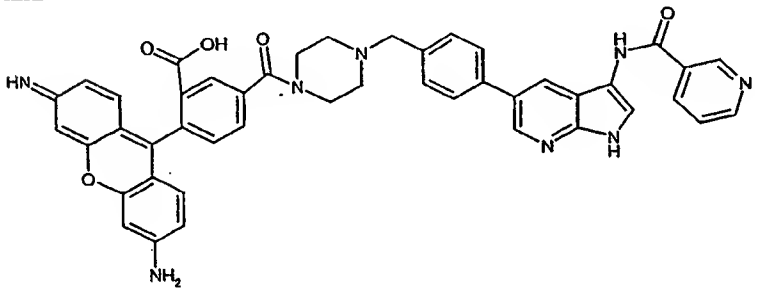


The compounds of the present invention may contain one or more asymmetric carbon atoms and may exist in racemic and optically active forms. All of these compounds and diastereomers are contemplated to be within the scope of the present invention.

The present compounds can also be formulated as pharmaceutically acceptable salts and complexes thereof. Pharmaceutically acceptable salts are non-toxic salts in the amounts and concentrations at which they are administered.

Pharmaceutically acceptable salts include acid addition salts such as those containing sulfate, hydrochloride, fumarate, maleate, phosphate, sulfamate, acetate, citrate, lactate, tartrate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, cyclohexylsulfamate and quinate. Pharmaceutically acceptable salts can be obtained from acids such as hydrochloric acid, maleic acid, sulfuric acid,

phosphoric acid, sulfamic acid, acetic acid, citric acid, lactic acid, tartaric acid, malonic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, cyclohexylsulfamic acid, fumaric acid, and quinic acid.

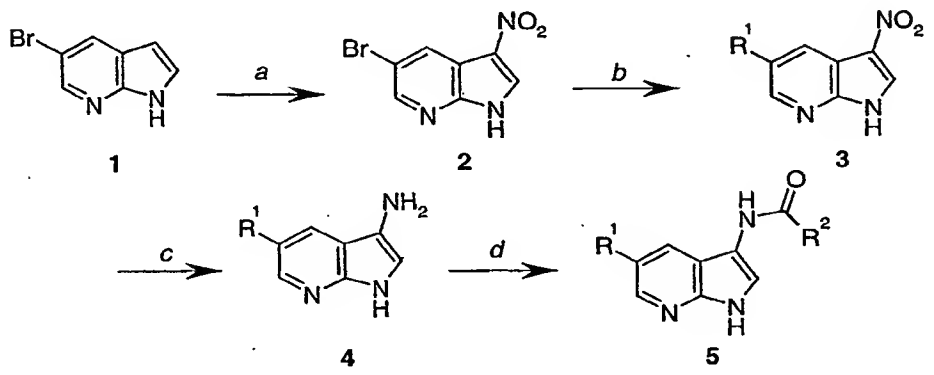
Pharmaceutically acceptable salts also include basic addition salts such as those containing benzathine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumine, procaine, aluminum, calcium, lithium, magnesium, potassium, sodium, ammonium, alkylamine, and zinc, when acidic functional groups, such as carboxylic acid or phenol are present.

Compounds such as formula (I) can be prepared by general methods from known or commercially available starting materials. Several methods for the preparation of compounds of formula (I) are shown below.

Compounds of formula (I) wherein R^1 is not sensitive to mild hydrogenation conditions can be prepared according to Scheme I. 5-Bromo-1*H*-pyrrolo[2,3-*b*]pyridine (**1**) (Mazeas,*Heterocylces* 1999. 50: 1-65-1080.) can be nitrated by several methods, for example with fuming nitric acid, or mixtures of nitric and sulfuric acids to provide compound **2**. Bromide **2** can then be transformed into **3** by the use of a variety of boronic acids (many commercially available) by standard procedures, for example using tetrakis(triphenylphosphine)palladium as catalyst in *N,N*-dimethylformamide / ethanol / aqueous 2M potassium carbonate at 100 °C. Alternatively, the boronic acid in the above example may be substituted for various boronic esters, for example pinacolate (4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl) or related boronic esters with no change in the course of the reaction. Nitro compound **3** can then be reduced to the corresponding amine **4** using heterogeneous hydrogenation, for example with palladium on carbon in the presence of 1 atmosphere of hydrogen gas in methanol. The amine **4** can then be acylated with a variety of acylating agents (many commercially available) to provide **5** by several standard methods, for example by treatment with acyl chorides or chloroformates in pyridine at various temperatures or by treatment with isocyanates in pyridine at various temperatures or by treatment with acid anhydrides in pyridine at various temperatures or by treatment with carboxylic acids in the presence of benzotraizol-1-

yloxy-tris(dimethylamino)phosphonium hexafluorophosphate (BOP) and triethylamine in *N,N*-dimethylformamide.

Scheme I

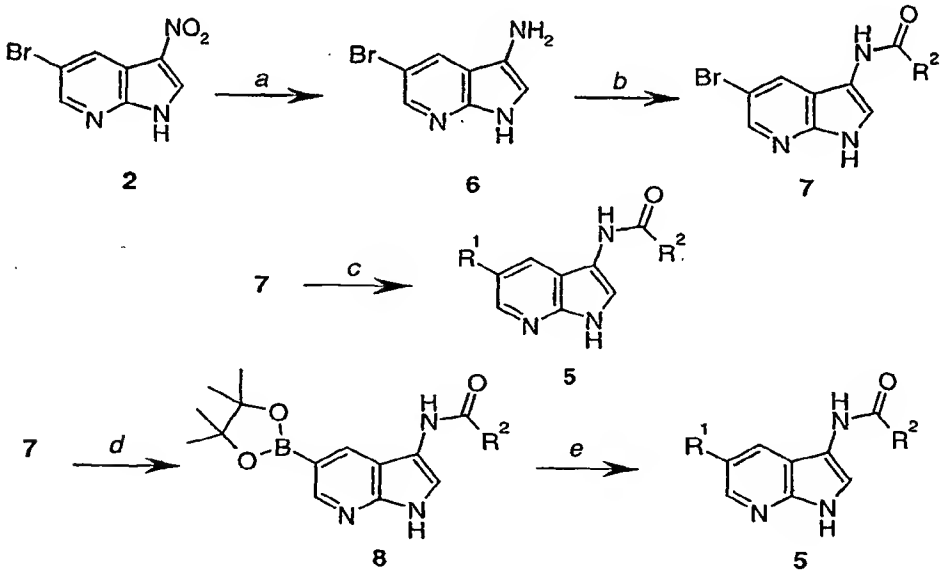


(*a*) fuming nitric acid, 0 °C. (*b*) $R^1B(OH)_2$, $(PPh_3)_4Pd$, DMF/EtOH/aq. 2M K_2CO_3, 100 °C. (*c*) H_2, Pd/C, MeOH, rt. (*d*) R^2COCl, pyr, rt; or R^2CNO, pyr, rt; or $(R^2CO)_2O$, pyr, rt; or R^2CO_2H, BOP, Et_3N, DMF, rt.

Compounds of formula (I) wherein R' is sensitive to mild hydrogenation conditions or wherein $R^1B(OH)_2$ or related reagents are unavailable, can be prepared according to Scheme II. 5-Bromo-3-nitro-1*H*-pyrrolo[2,3-*b*]pyridine (2) can be reduced to amine **6**, for example by stannous chloride in glacial acetic acid and 12M hydrochloride acid at 80 °C. The amine **6** can then be actylated with a variety of acylating agents (many commercially available) to provide **5** by several standard methods, for example by treatment with acyl chorides or chloroformates in pyridine at various temperatures or by treatment with isocyanates in pyridine at various temperatures or by treatment with acid anhydrides in pyridine at various temperatures or by treatment with carboxylic acids in the presence of benzotraizol-1-yloxy-tris(dimethylamino)phosphonium hexafluorophosphate (BOP) and triethylamine in *N,N*-dimethylformamide. Amide **7** can then be transformed to **5** by the use of a variety of boronic acids (many commercially available) by standard procedures, for example using tetrakis(triphenylphosphine)palladium as catalyst in

N,N-dimethylformamdide / ethanol / aqueous 2M potassium carbonate at 100 °C. Alternatively, the boronic acid in the above example may be substituted for various boronic esters, for example pinacolate (4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl) or related esters with no change in the course of the reaction. If the desired R^1 boronic acids or boronic esters are not readily available, then **7** can be converted to **8**, for example by bis(pinacolato)diboron, potassium acetate and [1,1'-bis(diphenylphosphino)-ferrocene]palladium(II) chloride in dimethylsulfoxide at 100 °C. Boronate **8** can then be converted to **5** by the use of a variety of aryl or heteroaryl chlorides or bromides or iodides, (many commercially available) by standard procedures, for example using tetrakis(triphenylphosphine)palladium as catalyst in *N,N*-dimethylformamdide / ethanol / aqueous 2M potassium carbonate at 100 °C.

Scheme II



(*a*) $SnCl_2$, HOAc, 12M HCl, 80 °C. (*b*) R^2COCl, pyr, rt; or R^2CNO, pyr, rt; or $(R^2CO)_2O$, pyr, rt; or R^2CO_2H, BOP, Et_3N, DMF, rt. (*c*) $R^1B(OH)_2$, $(PPh_3)_4Pd$, DMF/EtOH/aq. 2M K_2CO_3, 100 °C. (*d*) bis(pinacolato)diboron, $Pd(dppf)Cl_2$, KOAc, DMSO, 100 °C. (*e*) R^1Br, $(PPh_3)_4Pd$, DMF/EtOH/aq. 2M K_2CO_3, 100 °C.

Alternatively to the routes above, the organoboron compounds could be replaced with other organometallic compounds suitable for cross-coupling reactions such as stannanes, silanes, oragnozincs, cuprates, or organomagnesium reagents.

While not intended to be limiting in any way, the following examples illustrate the embodiments of the present invention.

Example 1

Preparation of *N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide

a) 5-Bromo-3-nitro-1*H*-pyrrolo[2,3-*b*]pyridine

5-Bromo-1-*H*-pyrrolo[2,3-*b*]pyridine (4.4 g, 22.3 mmol) was added in portions to fuming nitric acid (25 mL) at 0 °C over 15 min. The solution was allowed to stir at 0 °C for 1 h, then was poured into ice water. The resulting solid was filtered and dried to provide 4.5 g (83%) of the title compound. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 8.90 (s, 1H), 8.56-8.54 (m, 2H); ESIMS m/z = 242.0, 244.0 (M+1).

b) 3-Nitro-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine

Phenylboronic acid (1.10 g, 9.0 mmol, 1.5 equiv), tetrakis(triphenylphosphine)palladium (346 mg, 0.3 mmol, 0.05 equiv) and 5-bromo-3-nitro-1*H*-pyrrolo[2,3-*b*]pyridine (1.45 g, 6.0 mmol, 1.0 equiv) were combined in 2/1/1 DMF/EtOH/aq. 2M K_2CO_3 (40 mL) and the mixture was heated to reflux for 16 h. The reaction mixture was cooled, poured into H_2O and extracted with EtOAc. The organic extracts were combined, washed with brine, dried over $MgSO_4$, filtered and the filtrate was concentrated. The residue was purified by column chromatography (SiO_2, 2/1 EtOAc/hexanes to EtOAc) to give a solid which triturated with acetone to provide 1.03 g (72%) of the title compound. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 8.89 (s, 1H), 8.76 (d, J = 2.2, 1H), 8.59 (d, J = 2.3, 1H), 7.77 (d, J = 7.2, 2H), 7.54 (t, J = 7.3, 2H), 7.45 (t, J = 7.4, 1H); ESIMS m/z = 240.0 (M+1).

c) 3-Amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine

3-Nitro-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (250 mg, 1.05 mmol) and 5% Pd/C (100 mg) were hydrogenated at 1 atm in MeOH (30 mL) overnight. The mixture was filtered through Celite and the filtrate was concentrated. The residue was partitioned between 1M NaOH and CH_2Cl_2 and extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and concentrated to give 202 mg (92%) of the title compound. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.69 (s, 1H), 8.42 (d, J = 2.1, 1H), 8.22 (d, J = 1.9, 1H), 7.68 (d, J = 7.1, 2H), 7.48 (t, J = 7.5, 2H), 7.34 (t, J= 7.3, 1H), 6.69 (d, J = 2.1, 1H), 4.47 (brs, 2H).

d) *N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide

3-Amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride (25 mg, 0.1 mmol, 1.0 equiv) was dissolved in pyridine (0.3 mL), benzoyl chloride (15 mL, 0.12 mmol, 1.2 equiv) was added and the mixture was heated to 80 °C for 18 h. The reaction mixture was cooled, concentrated and the resiude purified by reverse-phase HPLC to give 5 mg (16%) of the title compound. ^{1}H NMR (400 MHz, CD_3OD) δ 8.95 (s, 1H), 8.62 (brs, 1H), 8.07-8.00 (m, 3H), 7.74 (dd, J= 9.4, 1.4, 2H), 7.63-7.47 (m, 5H), 7.43 (tt, J = 4.4, 1.1, 1H); ESIMS m/z = 314.4 (M+1).

Example 2

Preparation of *N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Butyric anhydride (33 µl, 0.202 mmol, 1.0 equiv) was added to a solution of the 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride (50 mg, 0.203 mmol, 1.0 equiv) in pyridine (0.5 mL). The reaction mixture was stirred at ambient temperature for 2 h and concentrated. Purification by column chromatography (2% MeOH in CH_2Cl_2) afforded 20 mg (36%) of the title compound. ^{1}H NMR ($CD_3S(O)CD_3$) δ 11.6 (s, 1H), 10.2 (s, 1H), 8.76 (d, 1H), 8.05 (d, 1H), 7.94 (d, 2H), 7.74 (t, 2H), 7.61 (t, 1H), 2.60 (t, 2H), 1.89 (m, 2H), 1.18 (t, 3H); APCIMS m/z = 280 (M+1).

Example 3

Preparation of (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-carbamic acid ethyl ester

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and ethyl chloroformate provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.58 (s, 1H), 8.52 (s, 1H), 7.70-7.63 (m, 3H), 7.50 (t, J = 7.4, 2H), 7.40 (t, J = 7.1, 1H), 4.23 (q, J = 7.1, 2H), 1.33 (t, J= 6.9, 3H); ESIMS m/z = 282.0 (M+1).

Example 4

Preparation of 1-ethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-urea

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and ethyl isocyanate provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 8.66 (d, J = 1.6, 1H), 8.57 (s, 1H), 7.73-7.70 (m, 2H), 7.66 (s, 1H), 7.52 (t, J = 7.2, 2H), 7.44 (tt, J = 7.5, 1.2, 1H), 3.27 (q, J = 7.2, 2H), 1.17 (t, J= 7.2, 3H); ESIMS m/z = 281.2 (M+1).

Example 5

Preparation of 2-methoxy-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-acetamide

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and methoxyacetyl chloride provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.82 (d, J = 1.9, 1H), 8.61 (s, 1H), 7.93 (s, 1H), 7.72 (d, J = 1.0, 2H), 7.53 (t, J = 7.1, 2H), 7.43 (tt, J = 7.2, 1.2, 1H), 4.16 (s, 2H), 3.53 (s, 3H); ESIMS m/z = 282.2 (M+1).

Example 6

Preparation of 4-methoxy-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and 4-methoxybenzoyl chloride provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.81 (d, J = 1.9, 1H), 8.54 (d, J = 1.6, 1H), 7.98 (d, J = 6.9, 2H), 7.93 (s, 1H), 7.69 (d, J = 8.0, 2H), 7.48 (t, J = 7.8, 2H), 7.39 (t, J = 7.8, 1H), 7.02 (d, J = 7.9, 2H); ESIMS m/z = 344.4 (M+1).

Example 7

Preparation of *N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and nicotonyl chloride hydrochloride provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 9.29 (brs, 1H), 8.86 (brs, 1H), 8.81 (d, J = 1.8, 1H), 8.71 (d, J = 2.0, 1H), 8.60 (brs, 1H), 8.07 (s, 1H), 7.86-7.83 (m, 1H), 7.74-7.70 (m, 2H), 7.51 (t, J = 7.4, 2H), 7.41 (t, J = 6.8, 1H); ESIMS m/z = 315.2 (M+1).

Example 8

Preparation of *N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-isonicotinamide

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and isonicotonyl chloride hydrochloride provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.93 (brs, 2H), 8.78 (d, J = 1.9, 1H), 8.61 (brs, 1H), 8.31 (d, J = 5.6, 2H), 8.05 (s, 1H), 7.72 (dd, J = 7.5, 1.4, 2H), 7.51 (t, J = 7.3, 2H), 7.42 (tt, J = 7.5, 1.2, 1H); ESIMS m/z = 315.2 (M+1).

Example 9

Preparation of 4-acetylamino-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and 4-acetylaminobenzoyl chloride provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.97 (s, 1H), 8.63 (s, 1H), 8.05-7.97 (m, 3H), 7.76-7.72 (m, 4H), 7.53 (t, J = 7.3, 2H), 7.44 (t, J = 7.4, 1H), 2.17 (s, 3H); ESIMS m/z = 371.2 (M+1).

Example 10

Preparation of 3-dimethylamino-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and 3-dimethylaminobenzoyl chloride provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.96 (d, J = 1.9, 1H), 8.62 (d, J = 1.6, 1H), 8.07 (s, 1H), 7.90-7.87 (m, 1H), 7.82 (d, J= 7.0, 1H), 7.71 (d,

J= 7.0, 2H), 7.59 (t, *J* = 7.9, 1H), 7.51 (t, *J* = 7.7, 2H), 7.42 (tt, *J*= 7.4, 1.2, 1H), 3.21 (s, 6H); ESIMS m/z = 357.4 (M+1).

Example 11

Preparation of acetic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-ylcarbamoyl)-methyl ester

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and acetoxyacetyl chloride provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.69 (d, *J* = 1.9, 1H), 8.57 (s, 1H), 7.90 (s, 1H), 7.70 (d, *J* = 7.2, 2H), 7.51 (t, *J*= 7.9, 2H), 7.42 (t, *J* = 7.3, 1H), 4.81 (s, 2H), 2.19 (s, 3H); ESIMS m/z = 310.2 (M+1).

Example 12

Preparation of *N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-isobutyramide

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and isobutyric anhydride provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.81 (d, *J* = 1.9, 1H), 8.59 (d, *J* = 1.6, 1H), 7.97 (s, 1H), 7.73-7.70 (m, 2H), 7.53 (t, *J*= 7.3, 2H), 7.44 (tt, *J* = 7.4, 1.2, 1H), 2.80 (sept, *J* = 6.8, 1H), 1.26 (d, *J* = 6.8, 6H); ESIMS m/z = 280.2 (M+1).

Example 13

Preparation of Benzo[1,3]dioxole-5-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and piperonyloyl choride provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 8.67 (d, *J* = 2.1, 1H), 8.57 (d, *J* = 2.1, 1H), 7.94 (s, 1H), 7.76-7.73 (m, 2H), 7.64 (dd, *J* = 8.1, 1.8, 1H), 7.58 (d, *J* = 1.7, 1H), 7.52 (t, *J* = 7.3, 2H), 7.38 (t, *J*= 7.4, 1H), 7.08 (d, *J*= 8.2, 1H), 6.14 (s, 2H); ESIMS m/z = 358.2 (M+1).

Example 14

Preparation of Pyrazine-2-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and pyrazine-2-carbonyl chloride provided the title compund. ESIMS m/z = 315.2 (M+).

Example 15

Preparation of Thiophene-2-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

Following the procedure for Example 1d, starting with 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and thiophene-2-carbonyl chloride provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.82 (d, *J* = 1.9, 1H), 8.58 (d, *J* = 1.6, 1H), 7.97 (dd, *J* = 3.7, 1.0, 1H), 7.94 (s, 1H), 7.75 (dd, *J* = 5.0, 1.1, 1H), 7.74-7.70 (m, 2H), 7.53-7.48 (m, 2H), 7.42 (tt, *J* = 7.4, 1.2, 1H), 7.21 (dd, *J* = 5.0, 3.8, 1H); ESIMS m/z = 320.0 (M+1).

Example 16

Preparation of (1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 1d, starting with 3-amino-1*H*-pyrrolo[2,3-*b*]pyridine hydrochloride and nicotonyl chloride hydrochloride provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 9.29 (d, *J* = 2.0, 1H), 8.88 (dd, *J* = 5.2, 1.5, 1H), 8.79 (dd, *J*= 8.0, 1.2, 1H), 8.74 (dt, *J* = 8.0, 2.0, 1H), 8.42 (d, *J* = 4.6, 1H), 8.13 (s, 1H), 7.87 (ddd, *J* = 8.0, 5.3, 0.6, 1H), 7.49 (dd, *J*= 8.0, 5.6, 1H).

Example 17

Preparation of *N*-(5-(3-acetamido-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

a) 3-amino-5-bromo-1*H*-pyrrolo[2,3-*b*]pyridine

5-Bromo-3-nitro-1*H*-pyrrolo[2,3-*b*]pyridine (4.5 g, 18.5 mmol, 1.0 equiv) was dissolved in glacial acetic acid (160 mL) at 85 °C, and a solution of tin(II) chloride dihydrate (17.5g, 92.5 mmol, 5.0 equiv) in conc. hydrochloric acid (18 mL) was added over 10 min. The mixture was stirred at 85 °C for 1 h, then cooled, poured into ice water and made basic by addition of 50% NaOH. The basic aqueous phase was then extracted with CH_2Cl_2, the organic extracts were combined, dried ($MgSO_4$) and concentrated to give 2.4 g (61%) of the title compound. . ^{1}H NMR (400

MHz, $CD_3S(O)CD_3$) δ 10.87 (s, 1H), 8.16 (d, *J* = 2.0, 1H), 8.13 (d, *J*= 2.1, 1H), 6.72 (d, *J* = 2.1, 1H), 4.40 (br s, 2H); ESIMS m/z = 212.0, 214.0 (M+1).

b) *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Butyric anhydride (1.16 mL, 7.1 mmol, 1.0 equiv) was added to a solution of 3-amino-5-bromo-1*H*-pyrrolo[2,3-*b*]pyridine (1.50 g, 7.1 mmol, 1 equiv) in CH_2Cl_2 (10 mL) and pyridine (5 mL). The mixture was stirred at rt for 2 h, then the volatiles were removed and the residue was partitioned between H_2O and EtOAc. The aqueous layer was extracted with EtOAc, the combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated to give a solid which was triturated with EtOAc to provide 1.31 g (65%) of the title compound. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 9.92 (s, 1H), 8.42 (d, *J* = 2.1, 1H), 8.26 (d, *J* = 2.1, 1H), 7.81 (d, *J* = 2.4, 1H), 2.33 (t, *J* = 7.4, 2H), 1.64 (sext, *J* = 7.4, 2H), 0.93 (t, *J* = 7.3, 2H); ESIMS m/z = 282.0, 284.0 (M+1).

c) *N*-(5-(3-acetamide-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

N-(5-Bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide (28 mg, 0.1 mmol, 1.0 equiv), tetrakis(triphenylphosphine)palladium (5.8 mg, 0.005 mmol, 0.05 equiv) and 3-acetamidobenzeneboronic acid (26.8 mg, 0.15 mmol, 1.5 equiv) were combined in 2/1/1 DMF/EtOH/aq. 2M K_2CO_3 (0.75 mL) and the mixture was heated to 100 ^{0}C for 15 h. The reaction mixture was cooled, concentrated, and the residue was purified by reverse phase HPLC to give the title compound. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 8.81 (d, *J* = 1.8, 1H), 8.56 (s, 1H), 8.06 (s, 1H), 7.98 (s, 1H), 7.43-7.38 (m, 3H), 2.47 (t, *J* = 7.3, 2H), 2.17 (s, 3H), 1.78 (sext, *J* = 7.4, 2H), 1.04 (t *J* = 7.4, 3H).

Example 18

Preparation of *N*-(5-(4-carboxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-carboxybenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.04 (s, 1H), 8.63 (s, 2H),

8.07 (d, J = 8.6, 2H), 7.87-7.83 (m, 3H), 2.37 (t, J = 7.3, 2H), 1.66 (sext, J = 7.3, 2H), 0.95 (t, J = 7.3, 3H).

Example 19

Preparation of *N*-(5-(4-dimethylamino-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-dimethylaminobenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 11.7 (s, 1H), 10.09 (s, 1H), 8.66 (s, 1H), 5.58 (s, 1H), 7.89 (d, J = 2.2, 1H), 7.69 (d, J = 8.7, 2H), 7.17 (d, J = 8.4, 2H), 2.38(t, J = 7.3, 2H), 1.66 (sext, J = 7.3, 2H), 0.95 (t, J = 7.3, 3H).

Example 20

Preparation of *N*-(5-(3-hydroxymethyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 3-hydroxymethylbenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.07 (s, 1H), 8.61 (d, J = 2.0, 1H), 8.57 (d, J = 2.0, 1H), 7.87 (d, J = 2.4, 1H), 7.69 (s, 1H), 7.59 (d, J = 7.8, 1H), 7.46 (t, J = 7.7, 1H), 7.33 (d, J= 7.6, 1H), 2.38 (t, J = 7.3, 2H), 1.66 (sext, J = 7.3, 2H), 0.95 (t, J = 7.3, 3H).

Example 21

Preparation of *N*-(5-(4-acetyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-acetylbenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.04 (s, 1H), 8.64 (s, 1H), 8.63 (s, 1H), 8.09 (d, J= 8.4, 2H), 7.89-7.85 (m, 3H), 2.38 (d, J = 7.3, 2H), 1.68 (d, J = 7.3, 2H), 0.95 (t, J = 7.3, 3H).

Example 22

Preparation of *N*-(5-(3-methyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 3-methylbenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.84 (d, J = 1.8, 1H), 8.57 (d, J = 1.7, 1H), 7.98 (s, 1H), 7.53-7.45 (m, 2H), 7.37 (t, J = 7.6, 1H), 7.25 (d, J = 7.4, 1H), 2.47 (t, J = 7.3, 2H), 2.44 (s, 3H), 1.78 (sext, J = 7.3, 2H), 1.04 (t, J = 7.3, 3H).

Example 23

Preparation of *N*-(5-(3-fluoro-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-1*H*-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 3-fluorobenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.74 (d, J = 1.9, 1H), 8.59 (d, J = 1.9, 1H), 7.95 (s, 1H), 7.55-7.45 (m, 3H), 7.20-7.12 (m, 1H), 2.47 (t, J = 7.3, 2H), 1.78 (d, J = 7.3, 2H), 1.04 (t, J = 7.3, 3H).

Example 24

Preparation of *N*-(5-(3-chloro-phenyl)-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 3-chlorobenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.68 (d, J = 2.0, 1H), 8.56 (d, J = 1.9, 1H), 7.93 (s, 1H), 7.74 (t, J = 1.9, 1H), 7.64 (ddd, J = 7.7, 1.6, 1.1, 1H), 7.50 (t, J = 7.9, 1H), 7.42 (ddd, J = 8.0, 2.0, 1.1, 1H), 2.47 (t, J = 7.3, 2H), 1.78 (sext, J = 7.3, 1H), 1.04 (t, J = 7.3, 1H); ESIMS m/z = 314.2 (M+1).

Example 25

Preparation of *N*-(5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-hydroxybenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.89 (d, J = 1.8, 1H), 8.55 (d, J =1.8, 1H), 8.00 (s, 1H), 7.56-7.53 (m, 2H), 6.97-6.93 (m, 2H), 2.48 (t, J = 7.3, 2H), 1.78 (sext, J = 7.3, 2H), 1.04 (t, J = 7.3, 3H); ESIMS m/z = 296.2 (M+1).

Example 26

Preparation of *N*-(5-(4-cyano-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-cyanobenzeneboronic acid provided

the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.66 (s, 1H), 8.60 (s, 1H), 7.92-7.83 (m, 5H), 2.47 (t, *J* = 7.3, 2H), 1.78 (sext, *J* = 7.3, 2H), 1.04 (t, *J* = 7.3, 3H); ESIMS m/z = 305.2 (M+1).

Example 27

Preparation of *N*-(5-(pyridin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and pyridine-3-boronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.03 (s, 1H), 9.10 (d, *J* = 2.0, 1H), 8.75-8.71 (m, 1H), 8.65 (d, *J* = 2.2, 1H), 8.60 (d, *J* = 2.0, 1H), 7.87-7.77 (m, 2H), 2.37 (t, *J* = 7.3, 2H), 1.66 (sext, *J* = 7.3, 2H), 0.95 (t, *J* = 7.3, 3H); ESIMS m/z = 281.2 (M+1).

Example 28

Preparation of *N*-(5-(pyridin-4-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and pyridine-4-boronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 8.86-8.82 (m, 3H), 8.78 (d, *J* = 2.2, 1H), 8.43 (d, *J* = 7.0, 2H), 7.85 (s, 1H), 2.49 (t, *J* = 7.3, 2H), 1.79 (sext, *J* = 7.3, 2H), 1.05 (t, *J* = 7.3, 3H); ESIMS m/z = 281.2 (M+1).

Example 29

Preparation of *N*-(5-(3-carboxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 3-carboxybenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.08 (s, 1H), 8.63 (s, 1H), 8.60 (s, 1H), 8.29 (t, *J* = 1.7, 1H), 8.01-7.95 (m, 2H), 7.95 (s, 1H), 7.64 (t, *J* = 7.8, 1H), 2.36 (t, *J* = 7.3, 2H), 1.66 (sext, *J* = 7.3, 2H), 0.95 (t, *J* = 7.3, 3H); ESIMS m/z = 324.2 (M+1).

Example 30

Preparation of *N*-(5-(4-methylsulfonyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-methylsulfonylbenzeneboronic acid

provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.81 (d, J = 2.0, 1H), 8.69 (d, J = 1.9, 1H), 8.11 (d, J = 6.6, 2H), 8.01-7.97 (m, 3H), 2.48 (t, J = 7.3, 2H), 1.78 (sext, J = 7.3, 2H), 1.05 (t, J = 7.3, 3H); ESIMS m/z = 358.4 (M+1).

Example 31

Preparation of *N*-(5-(4-chloro-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-chlorobenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.65 (d, J = 2.0, 1H), 8.55 (d, J = 2.0, 1H), 7.92 (s, 1H), 7.70-7.50 (m, 5H), 2.46 (t, J = 7.3, 2H), 1.77 (sext, J = 7.3, 2H), 1.04 (t, J = 7.3, 3H); ESIMS m/z = 314.2 (M+1).

Example 32

Preparation of *N*-(5-(4-hydroxymethyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-hydroxymethylbenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.88 (d, J = 1.9, 1H), 8.62 (d J = 1.7, 1H), 8.00 (s, 1H), 7.72 (d, J = 8.3, 2H), 7.54 (d, J = 8.1, 2H), 4.70 (s, 2H), 2.48 (t, J = 7.3, 2H), 1.79 (sext, J = 7.3, 2H), 1.05 (t, J = 7.3, 3H); ESIMS m/z = 310.2 (M+1).

Example 33

Preparation of *N*-(5-(3,4-dimethoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 3,4-dimethoxybenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, CD_3CN) δ 8.79 (d, J = 1.7, 1H), 8.72 (s, 1H), 8.53 (d, J = 1.7, 1H), 8.01 (s, 1H), 7.78 (brs, 1H), 7.21 (s, 1H), 7.18 (d, J = 8.0, 1H), 7.05 (d, J = 8.7, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 2.45 (t, J = 7.3, 2H), 1.76 (sext, J = 7.3, 2H), 1.03 (t, J = 7.3, 3H); ESIMS m/z = 340.4 (M+1).

Example 34

Preparation of *N*-(5-(thiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

a) *N*-(5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1*H*-pyrrolo[3,2-*b*]pyridin-3-yl)-butyramide

N-(5-Bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide (500 mg, 1.8 mmol, 1.0 equiv), bis(pinacolato)diboron (450 mg, 1.8 mmol, 1.0 equiv) and potassium acetate (521 mg, 5.3 mmol, 3.0 equiv) were dissolved in DMSO (10 mL) and the solution was degassed. Solid $PdCl_2$(dppf) (41 mg, 0.05 mmol, 0.03 equiv) was added and the mixture was heated to 100 °C for 16 h. The reaction mixture was then cool, poured into H_2O and EtOAc and filtered through Celite. The aqueous phase was extracted with EtOAc, the combined organic extracts were washed with H_2O and brine, dried over $MgSO_4$ and concentrated to give a brown solid which was triturated with EtOAc to provide 210 mg (36%) the title compound. . ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.06 (s, 1H), 8.62 (s, 1H), 8.44 (d, *J* = 1.4, 1H), 7.79 (d, *J* = 1.3, 1H), 2.34 (t, *J* = 7.3, 2H), 1.63 (sext, *J* = 7.4, 2H), 1.33 (s, 12H), 0.93 (t, *J* = 7.3, 3H).

b) *N*-(5-(thiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

N-(5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1*H*-pyrrolo[3,2-*b*]pyridin-3-yl)-butyramide (36 mg, 0.1 mmol, 1.0 equiv), tetrakis(triphenylphosphine)palladium (5.8 mg, 0.005 mmol, 0.05 equiv) and 3-bromothiophene (15 µL, 0.15 mmol, 1.5 equiv) were combined in 2/1/1 DMF/EtOH/aq. 2M K_2CO_3 (0.75 mL) and the mixture was heated to 100 °C for 15 h. The reaction mixture was cooled, concentrated, and the residue was purified by reverse phase HPLC to give the title compound. ^{1}H NMR (400 MHz, CD_3OD) δ 8.89 (d, *J* = 1.8, 1H), 8.67 (s, 1H), 7.97 (s, 1H), 7.81-7.78 (m, 1H), 7.61 (dd, *J* = 5.0, 2.9, 1H), 7.56 (dd, *J* = 5.0, 1.4, 1H), 2.48 (t, *J* = 7.3, 2H), 1.78 (sext, *J* = 7.3, 2H), 1.04 (t, *J* = 7.3, 3H), ESIMS m/z = 286.0 (M+1).

Example 35

Preparation of *N*-(5-(3-aminophenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 34b, starting from *N*-(5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1*H*-pyrrolo[3,2-*b*]pyridin-3-yl)-butyramide and 3-bromoaniline provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ

8.68 (d, J = 2.0, 1H), 8.58 (d, J = 2.0, 1H), 7.89 (s, 1H), 7.83-7.80 (m, 1H), 7.73-7.65 (m, 2H), 7.45-7.40 (m, 1H), 2.47 (t, J = 7.3, 2H), 1.78 (sext, J = 7.3, 2H), 1.04 (t, J = 7.3, 3H); ESIMS m/z = 295.2 (M+1).

Example 36

Preparation of *N*-(5-(4-aminomethylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 34b, starting from *N*-(5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1*H*-pyrrolo[3,2-*b*]pyridin-3-yl)-butyramide and 4-bromobenzylamine provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 8.75 (d, J = 1.9, 1H), 8.60 (d, J = 1.8, 1H), 7.92 (s, 1H), 7.81 (d, J = 8.3, 2H), 7.61 (d, J = 8.2, 2H), 4.20 (s, 2H), 2.47 (t, J = 7.3, 2H), 1.78 (sext, J = 7.3, 2H), 1.04 (t, J = 7.3, 3H); ESIMS m/z = 309.4 (M+1).

Example 37

Preparation of *N*-(5-(3-sulfamoylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 34b, starting from *N*-(5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1*H*-pyrrolo[3,2-*b*]pyridin-3-yl)-butyramide and 3-bromobenzenesulfonamide provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)\ CD_3$) δ 10.10 (s, 1H), 8.59 (s, 2H), 8.17 (s, 1H), 7.96 (d, J = 7.8, 1H), 7.87 (d, J = 2.4, 1H), 7.83 (d, J = 7.9, 1H), 7.71 (t, J = 7.8, 1H), 7.44 (s, 1H), 2.38 (t, J = 7.3, 2H), 1.66 (sext, J = 7.3, 2H), 0.95 (t, J = 7.3, 3H); ESIMS m/z = 359.2 (M+1).

Example 38

Preparation of *N*-(5-(4-sulfamoylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 34b, starting from *N*-(5-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1*H*-pyrrolo[3,2-*b*]pyridin-3-yl)-butyramide and 4-bromobenzenesulfonamide provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)\ CD_3$) δ 10.02 (s, 1H), 8.61 (d, J = 2.1, 1H), 8.58 (d, J = 2.1, 1H), 7.96-7.91 (m, 4H), 7.85 (d, J = 2.4, 1H), 7.41 (s, 2H), 2.37 (t, J = 7.3, 2H), 1.66 (sext, J = 7.3, 2H), 0.95 (t, J = 7.3, 3H); ESIMS m/z = 359.2 (M+1).

Example 39

Preparation of *N*-(5-(3-acetamido-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

a) *N*-(5-bromo-1*H*-pyrrolo[3,2-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17b starting from 3-amino-5-bromo-1*H*-pyrrolo[2,3-*b*]pyridine and nicotinoyl chloride hydrochloride provided the title compound. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.53 (s, 1H), 9.16 (d, *J* = 1.7, 1H), 8.77 (dd, *J*= 4.8, 2.0, 1H), 8.61 (d, *J* = 2.1, 1H), 8.36-8.30 (m, 2H), 7.99 (d, *J* = 2.6, 1H), 7.61-7.57 (m, 1H).

b) *N*-(5-(3-acetamido-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 3-acetamidobenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.68 (s, 1H), 10.07 (s, 1H), 9.21 (d, *J* = 2.0, 1H), 8.82 (d, *J* = 4.9, 1H), 8.61 (d, *J* = 2.1, 1H), 8.52 (d, *J* = 2.0, 1H), 8.44 (d, *J* = 8.0, 1H), 7.97 (d, *J* = 9.1, 1H), 7.68 (dd, *J* = 7.8, 5.0, 1H), 7.56-7.53 (m, 1H), 7.44-7.37 (m, 1H).

Example 40

Preparation of *N*-(5-(4-hydroxymethyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 4-hydroxymethylbenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.66 (s, 1H), 9.25 (d, *J* = 1.7, 1H), 8.84 (dd, *J*= 5.0, 1.6, 1H), 8.67 (d, *J* = 2.0, 1H), 8.59 (d, *J* = 2.2, 1H), 8.47 (d, *J* = 8.0, 1H), 8.00 (d, *J* = 2.5, 1H), 7.72 (dd, *J* = 4.1, 2.2, 2H), 7.45 (d, *J* = 8.2, 2H), 4.57 (s, 2H).

Example 41

Preparation of *N*-(5-(4-dimethylamino-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 4-dimethylaminobenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.61 (s, 1H), 9.21

(d, J = 1.7, 1H), 8.82 (dd, J = 4.9, 1.5, 1H), 8.60 (d, J = 2.0, 1H), 8.54 (d, J = 2.1, 1H), 8.45-8.41 (m, 1H), 7.96 (d, J = 2.5, 1H), 7.70-7.61 (m, 3H), 2.99 (s, 6H).

Example 42

Preparation of *N*-(5-(3,4-dimethoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 3,4-dimethoxybenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.56 (s, 1H), 9.19 (d, J = 1.7, 1H), 8.77 (dd, J = 4.8, 1.4, 1H), 8.59-8.55 (m, 2H), 8.36 (dt, J = 8.0, 1.8, 1H), 7.97 (s, 1H), 7.60 (dd, J = 8.5, 3.8, 1H), 7.28 (d, J = 2.0, 1H), 7.26-7.22 (m, 2H), 7.08 (d, J = 8.3, 1H), 3.88 (s, 3H), 3.81 (s, 3H).

Example 43

Preparation of *N*-(5-(3,4-(methylenedioxy)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 3,4-(methylenedioxy)benzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.53 (s, 1H), 9.18 (s, 1H), 8.80-8.75 (m, 1H), 8.57 (d, J = 2.0, 1H), 8.52 (d, J = 2.1, 1H), 8.35 (dt, J = 10.0, 2.0, 1H), 7.96 (d, J = 2.5, 1H), 7.69 (dd, J = 7.8, 4.8, 1H), 7.31 (d, J = 1.7, 1H), 7.20 (dd, J = 8.1, 1.8, 1H), 7.05 (d, J = 8.0, 1H), 6.08 (s, 2H).

Example 44

Preparation of *N*-(5-(thiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and thiophene-3-boronic acid provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 9.28 (dd, J = 2.0, 0.6, 1H), 8.86 (dd, J = 5.2, 1.6, 1H), 8.81 (d, J = 1.9, 1H), 8.70 (dt, J = 7.2, 1.8, 1H), 8.66 (d, J = 1.1, 1H), 8.04 (s, 1H), 7.86-7.81 (m, 1H), 7.75 (dd, J= 2.8, 1.4, 1H), 7.59-7.55 (m, 2H).

Example 45

Preparation of *N*-(5-(4-aminophenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 4-(4,4,5,5-tetramethyl-1,3,2-

dioxaborolan-2-yl)aniline provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 9.36 (d, *J* = 1.8, 1H), 8.94-8.89 (m, 2H), 8.83 (d, *J*= 2.0, 1H), 8.64 (d, *J* = 2.0, 1H), 8.07 (s, 1H), 8.00 (ddd, *J* = 8.1, 5.5, 0.7, 1H), 7.88 (dt, *J* = 8.3, 0.9, 2H), 7.53 (dt, *J* = 8.5, 1.8, 2H); ESIMS m/z = 330.4 (M+1).

Example 46

Preparation of *N*-(5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 3-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 9.26 (s, 1H), 8.86-8.83 (m, 2H), 8.66 (dt, *J* = 8.0, 1.8, 1H), 8.57 (s, 1H), 8.10 (s, 1H), 7.82 (dd, *J*= 8.0, 4.8, 1H), 7.27 (d, *J* = 2.0, 1H), 7.16 (dd, *J* = 8.2, 2.1, 1H), 6.94 (d, *J*= 8.2, 1H), 3.96 (s, 3H); ESIMS m/z = 361.2 (M+1)

Example 47

Preparation of *N*-(5-(3,5-dimethyl-4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 9.26 (s, 1H), 8.90 (d, *J* = 1.9, 1H), 8.85 (br d, *J* = 4.0, 1H), 8.68 (dt, *J* = 8.1, 2.0, 1H), 8.55 (d, *J* = 1.6, 1H), 8.09 (s, 1H), 7.83 (dd, *J* = 8.0, 5.2, 1H), 7.30 (s, 2H), 2.30 (s, 6H); ESIMS m/z = 359.2 (M+1).

Example 48

Preparation of *N*-(5-(naphthalen-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and naphthalene-2-boronic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10 71 (s, 1H), 9.26 (d, *J* = 2.0, 1H), 8.86-8.83 (m, 2H), 8.76 (d, *J* = 2.0, 1H), 8.51 (dt, *J* = 8.0, 1.4, 1H), 8.29 (s, 1H), 8.06-7.93 (m, 5H), 7.72 (dd, *J*= 7.9, 5.0, 1H), 7.59-7.52 (m, 2H); ESIMS m/z = 365.2 (M+1).

Example 49

Preparation of *N*-(5-(4-methoxyphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 4-methoxybenzeneboronic acid provided the title compund. ^{1}H NMR (400 MHz, CD_3OD) δ 9.33 (d, *J*= 2.0, 1H), 8.93-8.88 (m, 2H), 8.82 (dt, *J*= 8.0, 2.0, 1H), 8.56 (d, *J* = 1.8, 1H), 8.09 (s, 1H), 7.93 (dd, *J*= 7.9, 5.3, 1H), 7.62 (d, *J* = 8.8, 2H), 7.03 (d, *J*= 8.8, 2H), 3.84 (s, 3H); ESIMS m/z = 345.2 (M+1).

Example 50

Preparation of pyridine-2-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

3-Amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (42 mg, 0.2 mmol, 1.0 equiv), pyridine-2-carboxylic acid (24 mg, 0.2 mmol, 1.0 equiv) and Et_3N (84 µL, 0.6 mmol, 3.0 equiv) were combined in DMF (1 mL). BOP reagent (106 mg, 0.24 mmol, 1.2 equiv) was added and the mixture was stirred at rt for 16 h. The reaction mixture was then poured into H_2O and extracted with EtOAc. The combined organic extracts were washed with H_2O and brine, dried over $MgSO_4$ and concentrated. The reside was purified by reverse-phase HPLC to give 36 mg (57%) of the title compound. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 10.85 (s, 1H), 8.84-8.78 (m, 2H), 8.61 (d, *J* = 2.0, 1H), 8.21-8.16 (m, 1H), 8.13-7.95 (m, 2H), 7.78 (m, 2H), 7.71-7.65 (m, 1H), 7.55-7.49 (m, 1H), 7.41-7.37 (m, 1H).

Example 51

Preparation of 4-methyl-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 50, starting from 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine and 4-methylnicotinic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 9.08 (s, 1H), 8.79 (d, *J* = 5.9, 1H), 8.69 (d, *J* = 1.9, 1H), 8.61 (s, 1H), 8.15 (s, 1H), 7.98 (d, *J* = 5.9, 1H), 7.70 (d, *J* = 8.0, 2H), 7.51 (t, *J* = 7.3, 2H), 7.42 (t, *J*= 7.5, 1H), 2.78 (s, 3H); ESIMS m/z = 329.4 (M+1).

Example 52

Preparation of 6-methyl-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 50, starting from 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine and 6-methylnicotinic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 9.25 (d, *J* = 1.8, 1H), 8.90 (dd, *J* = 8.3, 2.9, 1H), 8.79 (d, *J*= 2.1, 1H), 8.61 (s, 1H), 8.08 (s, 1H), 7.96 (d, *J* = 8.3, 1H), 7.74 (d, *J* = 8.0, 2H), 7.52 (t, *J* = 7.3, 2H), 7.42 (t, *J* = 7.5, 1H), 2.84 (s, 3H); ESIMS m/z = 329.2 (M+1).

Example 53

Preparation of 3-hydroxy-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide

Following the procedure for Example 50, starting from 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine and 3-hydroxybenzoic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 8.91 (d, *J* = 1.8, 1H), 8.62 (s, 1H), 8.04 (s, 1H), 7.76-7.3 (m, 2H), 7.55-7.40 (m, 5H), 7.35 (t, *J* = 7.9, 1H), 7.04-7.01 (m, 1H); ESIMS m/z = 330.4 (M+1).

Example 54

Preparation of 6-(2-(pyrrolidin-1-yl)ethyl-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 50, starting from 3-amino-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine and 6-(2-pyrrolidin-1-yl)ethyl)pyridine carboxylic acid provided the title compund. ^{1}H NMR (400 MHz, $CD_3S(O)CD_3$) δ 9.44 (d, *J* = 1.6, 1H), 9.41 (s, 1H), 8.91 (d, *J* = 7.8, 1H), 8.77 (s, 1H), 8.28 (s, 1H), 8.03 (d, *J* = 8.2, 1H), 7.90-7.75 (m, 2H), 7.60-7.45 (m, 3H), 3.82-3.75 (m, 4H), 3.61-3.55 (m, 2H), 3.27-3.20 (m, 2H), 2.25-2.19 (m, 2H), 2.15-2.08 (m, 2H).

Example 55

Preparation of *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 3-formylbenzeneboronic acid provided the title compound. ESIMS m/z = 308.2 (M+1).

Example 56

Preparation of *N*-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-formylbenzeneboronic acid provided the title compound. ESIMS m/z = 308.2 (M+1).

Example 57

Preparation of *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 3-formylbenzeneboronic acid provided the title compound. ESIMS m/z = 343.2 (M+1).

Example 58

Preparation of *N*-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 4-formylbenzeneboronic acid provided the title compound. ESIMS m/z = 343.0 (M+1).

Example 59

Preparation of *N*-(5-(4-dimethylaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

N-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide (51 mg, 0.15 mmol, 1.0 equiv) and dimethylamine hydrochloride (61 mg, 0.75 mmol, 5 equiv) were combind in MeOH (1.5 mL). Glacial acetic acid (86 uL, 1.5 mmol, 10 equiv) was added, followed by sodium cyanoborohydride (38 mg, 0.6 mmol, 4.0 equiv) and the mixture heated to reflux for 5 h. The reaction mixture was cooled and concentrated and the residue purified by preparative HPLC to give the title compound. ESIMS m/z = 372.2 (M+1).

Example 60

Preparation of *N*-(5-(4-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and morpholine provided the title compound. ESIMS m/z = 414.2 (M+1).

Example 61

Preparation of *N*-(5-(4-(4-methylpiperazino)-methyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 4-methylpiperazine provided the title compound. ESIMS m/z = 427.3 (M+1).

Example 62

Preparation of *N*-(5-(4-piperidinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and piperidine provided the title compound. ESIMS m/z = 411.1 (M+1).

Example 63

Preparation of *N*-(5-(4-pyrrolidinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and pyrrolidine provided the title compound. ESIMS m/z = 398.2 (M+1).

Example 64

Preparation of *N*-(5-(4-methylaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and methylamine hydrochloride provided the title compound. ESIMS m/z = 358.2 (M+1).

Example 65

Preparation of *N*-(5-(4-diethanolaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and diethanolamine provided the title compound. ESIMS m/z = 432.4 (M+1).

Example 66

Preparation of *N*-(5-(4-(4-t-butoxycarbonyl)-piperazinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and *N*-boc-piperazine provided the title compound. ESIMS m/z = 513.4 (M+1).

Example 67

Preparation of *N*-(5-(3-(4-t-butoxycarbonyl)-piperazinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and *N*-boc-piperazine provided the title compound. ESIMS m/z = 513.6 (M+1).

Example 68

Preparation of *N*-(5-(3-dimethylaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and dimethylamine hydrochloride provided the title compound. ESIMS m/z = 372.2 (M+1).

Example 69

Preparation of *N*-(5-(3-(4-methylpiperazinomethyl)-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 4-methylpiperazine provided the title compound. ESIMS m/z = 427.2 (M+1).

Example 70

Preparation of *N*-(5-(3-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and morpholine provided the title compound. ESIMS m/z = 414.2 (M+1).

Example 71

Preparation of *N*-(5-(3-diethanolaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and diethanolamine provided the title compound. ESIMS m/z = 432.4 (M+1).

Example 72

Preparation of *N*-(5-(3-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 59, starting from *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and morpholine provided the title compound. ESIMS m/z = 379.2 (M+1).

Example 73

Preparation of *N*-(5-(3-(4-methylpiperazinomethyl)-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 59, starting from *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-methylpiperazine provided the title compound. ESIMS m/z = 392.4 (M+1).

Example 74

Preparation of *N*-(5-(4-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 59, starting from *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and morpholine provided the title compound. ESIMS m/z = 379.2 (M+1).

Example 75

Preparation of *N*-(5-(4-(4-methylpiperazinomethyl)-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide

Following the procedure for Example 59, starting from *N*-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide and 4-methylpiperazine provided the title compound. ESIMS m/z = 392.4 (M+1).

Example 76

Preparation of thiophene-3-carboxylic acid (5-(4-hydoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

a) 5-(4-Hydroxyphenyl)-3-nitro-1*H*-pyrrolo[2,3-*b*]pyridine

Following the procedure for Example 1b, starting from 5-bromo-3-nitro-1*H*-pyrrolo[2,3-*b*]pyridine and 4-hydroxybenzeneboronic acid provided the title compound. ESIMS m/z = 256.2 (M+1).

b) 3-Amino-5-(4-hydroxyphenyl)-1*H*-pyrrolo[2,3-*b*]pyridine

Following the procedure for Example 1c, starting from 5-(4-hydroxyphenyl)-3-nitro-1*H*-pyrrolo[2,3-*b*]pyridine provided the title compound. ESIMS m/z = 226.4 (M+1).

c) Thiophene-3-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

Following the procedure for Example 1d, starting from 3-amino-5-(4-hydroxyphenyl)-1*H*-pyrrolo[2,3-*b*]pyridine and thiophene-3-carbonyl chloride provided the title compound. ESIMS m/z = 336.2 (M+1).

Example 77

Preparation of furan-2-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

Following the procedure for Example 1d, starting from 3-amino-5-(4-hydroxyphenyl)-1*H*-pyrrolo[2,3-*b*]pyridine and furan-2-carbonyl chloride provided the title compound. ESIMS m/z = 320.0 (M+1).

Example 78

Preparation of *N*-((5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 1d, starting from 3-amino-5-(4-hydroxyphenyl)-1*H*-pyrrolo[2,3-*b*]pyridine and nicotonyl chloride hydrochloride provided the title compound. ESIMS m/z = 331.2 (M+1).

Example 79

Preparation of pyrrole-2-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

Following the procedure for Example 1d, starting from 3-amino-5-(4-hydroxyphenyl)-1*H*-pyrrolo[2,3-*b*]pyridine and pyrrole-2-carbonyl chloride provided the title compound. ESIMS m/z = 319.2 (M+1).

Example 80

Preparation of 2-methyl-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide

a) 5-(4-Hydroxy-3-methoxy-phenyl)-3-nitro-1*H*-pyrrolo[2,3-*b*]pyridine

Following the procedure for Example 1b, starting from 5-bromo-3-nitro-1*H*-pyrrolo[2,3-*b*]pyridine and 4-hydroxy-3-methoxybenzeneboronic acid provided the title compound. ESIMS m/z = 286.3 (M+1).

b) 3-amino-5-(4-Hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine

Following the procedure for Example 1c, starting 5-(4-hydroxy-3-methoxy-phenyl)-3-nitro-1*H*-pyrrolo[2,3-*b*]pyridine provided the title compound. ESIMS m/z = 256.2 (M+1).

c) 2-methyl-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide

Following the procedure for Example 1d, starting from 3-amino-5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine and 2-methylbenzoyl chloride provided the title compound. ESIMS m/z = 374.2 (M+1).

Example 81

Preparation of 2-chloro-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide

Following the procedure for Example 1d, starting from 3-amino-5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine and 2-chlorobenzoyl chloride provided the title compound. ESIMS m/z = 394.2 (M+1).

Example 82

Preparation of *N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-2-methoxybenzamide

Following the procedure for Example 1d, starting from 3-amino-5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine and 2-methoxybenzoyl chloride provided the title compound. ESIMS m/z = 390.2 (M+1).

Example 83

Preparation of pyrazine-2-carboxylic acid ((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

Following the procedure for Example 1d, starting from 3-amino-5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine and pyrazine-2-carbonyl chloride provided the title compound. ESIMS m/z = 362.2 (M+1).

Example 84

Preparation of 2-hydroxy-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide

Following the procedure for Example 50, starting from 3-amino-5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 2-hydroxybenzoic acid provided the title compound. ESIMS m/z = 376.2 (M+1).

Example 85

Preparation of pyrimidine-5-carboxylic acid-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

Following the procedure for Example 50, starting from 3-amino-5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine pyrimidine-5-carboxylic acid provided the title compound. ESIMS m/z = 362.2 (M+1).

Example 86

Preparation of 5-bromo-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 50, starting from 3-amino-5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 5-bromonicotinic acid provided the title compound. ESIMS m/z = 438.8 and 440.8.0 (M+1).

Example 87

Preparation of *N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-5-methyl-nicotinamide

Following the procedure for Example 50, starting from 3-amino-5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 5-methylnicotinic acid provided the title compound. ESIMS m/z = 375.2 (M+1).

Example 88

Preparation of *N*-((5-(benzothiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and benzothiophene-3-boronic acid provided the title compound. ESIMS m/z = 355.0 (M+1).

Example 89

Preparation of *N*-((5-(thiophen-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and thiophene-2-boronic acid provided the title compound. ESIMS m/z = 321.1 (M+1).

Example 90

Preparation of *N*-((5-(4-methylpiperazinophenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 4-(4-methylpiperazino)benzene-boronic acid provided the title compound. ESIMS m/z = 413.4 (M+1).

Example 91

Preparation of *N*-((5-(3-biphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and 3-biphenyl-boronic acid provided the title compound. ESIMS m/z = 391.2 (M+1).

Example 92

Preparation of *N*-((5-(benzofuran-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and benzofuran-2-yl-boronic acid provided the title compound. ESIMS m/z = 355.3 (M+1).

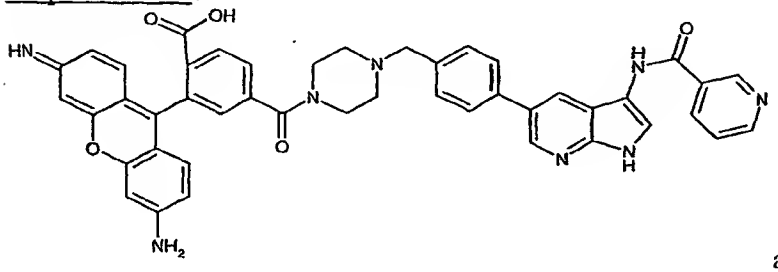
Example 93

Preparation of *N*-((5-(indol-5-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

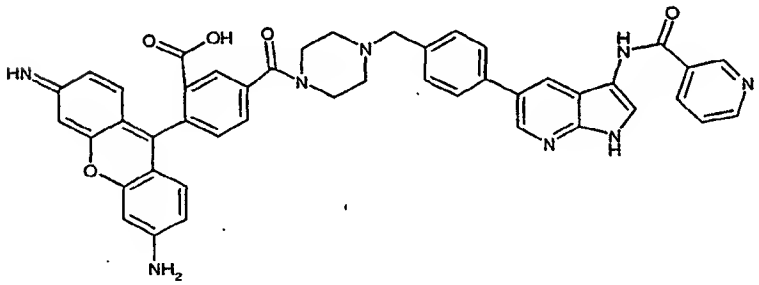
Following the procedure for Example 17c, starting from *N*-(5-bromo-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and indole-5-boronic acid provided the title compound. ESIMS m/z = 354.3 (M+1).

Example 94

Preparation of :



and



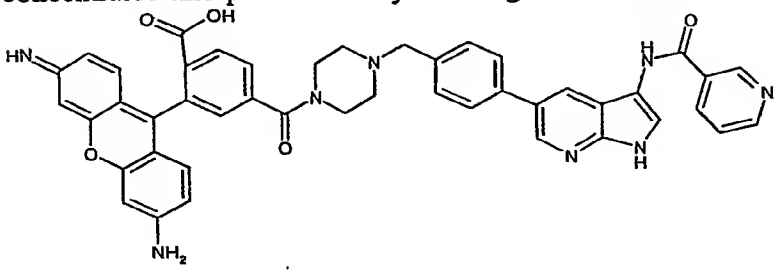
a) *N*-((5-(4-(Piperazin-1-yl-methyl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide

Following the procedure for Example 59, starting from *N*-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide and piperazine provided the title compound. ESIMS m/z = 413.0 (M+1).

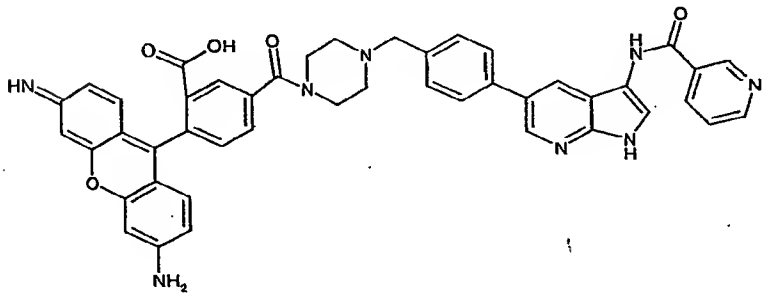
b)

A solution of *N*-((5-(4-(piperazin-1-yl-methyl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide in dimethylacetamide is treated with triethylamine and Rhodamine Green™ carboxylic acid, succinimidyl ester, hydrochloride (mixture of

5- and 6-isomers, from Molecular Probes, reagenet # R-6107). The solution is concentrated and purification by HPLC gives a mixture of:



and



With appropriate manipulation and protection of any chemical functionality, synthesis of the remaining compounds of Formula (I) is accomplished by methods analogous to those above.

In order to use a compound of Formula (I) or a pharmaceutically acceptable salt thereof for the treatment of humans and other mammals, it is normally formulated in accordance with standard pharmaceutical practice as a pharmaceutical composition.

The present ligands can be administered by different routes including intravenous, intraperitoneal, subcutaneous, intramuscular, oral, topical, transdermal, or transmucosal administration. For systemic administration, oral administration is preferred. For oral administration, for example, the compounds can be formulated into conventional oral dosage forms such as capsules, tablets and liquid preparations such as syrups, elixirs and concentrated drops.

Alternatively, injection (parenteral administration) may be used, e.g., intramuscular, intravenous, intraperitoneal, and subcutaneous. For injection, the compounds of the invention are formulated in liquid solutions, preferably, in physiologically compatible buffers or solutions, such as saline solution, Hank's

solution, or Ringer's solution. In addition, the compounds may be formulated in solid form and redissolved or suspended immediately prior to use. Lyophilized forms can also be produced.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, bile salts and fusidic acid derivatives. In addition, detergents may be used to facilitate permeation. Transmucosal administration, for example, may be through nasal sprays, rectal suppositories, or vaginal suppositories.

For topical administration, the compounds of the invention can be formulated into ointments, salves, gels, or creams, as is generally known in the art.
The amounts of various compounds to be administered can be determined by standard procedures taking into account factors such as the compound IC_{50}, EC_{50}, the biological half-life of the compound, the age, size and weight of the patient, and the disease or disorder associated with the patient. The importance of these and other factors to be considered are known to those of ordinary skill in the art.

Amounts administered also depend on the routes of administration and the degree of oral bioavailability. For example, for compounds with low oral bioavailability, relatively higher doses will have to be administered.

Preferably the composition is in unit dosage form. For oral application, for example, a tablet, or capsule may be administered, for nasal application, a metered aerosol dose may be administered, for transdermal application, a topical formulation or patch may be administered and for transmucosal delivery, a buccal patch may be administered. In each case, dosing is such that the patient may administer a single dose.

Each dosage unit for oral administration contains suitably from 0.01 to 500 mg/Kg, and preferably from 0.1 to 50 mg/Kg, of a compound of Formula (I) or a pharmaceutically acceptable salt thereof, calculated as the free base. The daily dosage for parenteral, nasal, oral inhalation, transmucosal or transdermal routes contains suitably from 0.01 mg to 100 mg/Kg, of a compound of Formula(I). A

topical formulation contains suitably 0.01 to 5.0% of a compound of Formula (I). The active ingredient may be administered from 1 to 6 times per day, preferably once, sufficient to exhibit the desired activity, as is readily apparent to one skilled in the art.

As used herein, "treatment" of a disease includes, but is not limited to prevention, retardation and prophylaxis of the disease. As used herein, "diseases" treatable using the present compounds include, but are not limited to leukemias, solid tumor cancers and metastases, lymphomas, soft tissue cancers, brain cancer, esophageal cancer, stomach cancer, pancreatic cancer, liver cancer, lung cancer, bladder cancer, bone cancer, prostate cancer, ovarian cancer, cervical cancer, uterine cancer, testicular cancer, kidney cancer, head cancer and neck cancer, chronic inflammatory proliferative diseases such as psoriasis and rheumatoid arthritis; proliferative cardiovascular diseases such as restenosis; prolifertive ocular disorders such as diabetic retinopathy; and benign hyperproliferative diseases such as hemangiomas.

Composition of Formula (I) and their pharmaceutically acceptable salts which are active when given orally can be formulated as syrups, tablets, capsules and lozenges. A syrup formulation will generally consist of a suspension or solution of the compound or salt in a liquid carrier for example, ethanol, peanut oil, olive oil, glycerine or water with a flavoring or coloring agent. Where the composition is in the form of a tablet, any pharmaceutical carrier routinely used for preparing solid formulations may be used. Examples of such carriers include magnesium stearate, terra alba, talc, gelatin, acacia, stearic acid, starch, lactose and sucrose. Where the composition is in the form of a capsule, any routine encapsulation is suitable, for example using the aforementioned carriers in a hard gelatin capsule shell. Where the composition is in the form of a soft gelatin shell capsule any pharmaceutical carrier routinely used for preparing dispersions or suspensions may be considered, for example aqueous gums, celluloses, silicates or oils, and are incorporated in a soft gelatin capsule shell.

Typical parenteral compositions consist of a solution or suspension of a compound or salt in a sterile aqueous or non-aqueous carrier optionally containing a

parenterally acceptable oil, for example polyethylene glycol, polyvinylpyrrolidone, lecithin, arachis oil or sesame oil.

Typical compositions for inhalation are in the form of a solution, suspension or emulsion that may be administered as a dry powder or in the form of an aerosol using a conventional propellant such as dichlorodifluoromethane or trichlorofluoromethane.

A typical suppository formulation comprises a compound of Formula (I) or a pharmaceutically acceptable salt thereof which is active when administered in this way, with a binding and/or lubricating agent, for example polymeric glycols, gelatins, cocoa-butter or other low melting vegetable waxes or fats or their synthetic analogs.

Typical dermal and transdermal formulations comprise a conventional aqueous or non-aqueous vehicle, for example a cream, ointment, lotion or paste or are in the form of a medicated plaster, patch or membrane.

Preferably the composition is in unit dosage form, for example a tablet, capsule or metered aerosol dose, so that the patient may administer a single dose.

No unacceptable toxological effects are expected when compounds of the present invention are administered in accordance with the present invention.

The biological activity of the compounds of Formula (I) are demonstrated by the tests indicated hereinbelow.

Chk1 Methods:

Streptavidin coated SPA beads, ATP and ^{33}P-ATP were obtained from Amersham Pharmacia Biotech, Biotin labeled peptide KVSRSGLYRSPSMPENLNRK(Biotin-xx)NH_2 was obtained from Affiniti Research Products Ltd, assay buffer reagents were obtained from Sigma-Aldrich Co.Ltd. fff84 well assay plates were obtained from Corning Inc. Assay buffer: 50 mM HEPES, 50 mM KCl, 5% Glycerol, 1 mM EGTA, 0.001% Tween-20; enzyme/peptide mix: 25 nM Chk1, 2.5μM biotin peptide, 7.5 mM 2-mercaptoethanol in assay buffer; ATP mix: 20μM ATP at 650kBq/mL, 5mM $MgCl_2$ in assay buffer.

Inhibitors of decreasing concentration, from 10μM were incubated at room temperature for 1 hour together with 5μL enzyme/peptide mix and 5μL ATP mix. The reaction was stopped with 5μL of 0.5M EDTA followed by a further addition of 65μL of 0.2mg/mL SPA beads. Plates were spun at 2500 rpm for 10 minutes and the amount of ^{33}P incorporated onto the peptide was quantified by a Wallac Trilux scintillation counter at a read time of 1 minute per well. IC50's were fitted to the data using SDM Explorer version 2.5 software (©GlaxoSmthKline Plc.).

Compounds capable of inhibiting Chk1 kinase can be identified with in vitro assays and cellular assays as described below. Variations of these assays would be obvious to those skilled in the art.

Expression of GST-Chk1:

A GST-Chk1 expression construct was constructed which has the glutathione-S-transferase gene fused to the amino terminus of Chk1 kinase via a linker containing a thrombin cleavage site. This construct was cloned into the Baculovirus expression vector, pFASTBAC, and this was used to make the viral stock for the subsequent infection. Spodoptera frugiperda cells (Sf9) were infected with the virus expressing the GST-Chk1 and the cells were grown for 3 days, then harvested and frozen down.

Purification of GST-Chk1:

The GST-Chk1 protein was purified as follows: An Sf9 cell pellet expressing GST-Chk1 was resuspended on ice in lysis buffer (50mM Tris-Cl, pH 7.5, 250mM $NaCl_2$, 1mM dithiothreitol (DTT), 0.1%Brij, 5% (v/v) protease inhibitor cocktail, 1mM sodium orthovanadate), cells were lysed by sonication and centrifuged at 100,000xg for 30min The supernatant was added to Glutathione Sepharose 4B, beads, equilibrated in wash buffer (20mM Tris-Cl, pH 7.0, 10mM $MgCl_2$, 100mM $NaCl_2$, 1mM DTT, 0.5%(v/v) protease inhibitor cocktail, 1mM sodium orthovanadate). The mixture was rocked for 30min The resin with the bound GST-Chk1 was spun down at 500xg for 5min and washed with 14mls of wash buffer. The beads were spun as above and resuspended in another 14mls of wash buffer. The suspension was transferred into a column and allowed to pack, then the wash buffer was allowed to flow through by gravity. The GST-Chk1 was eluted from the

column with 10mM Glutathione in 50mM Tris-Cl, pH 8.0 in 500ul fractions. Protein concentrations were determined on the fractions using Bio-Rad's Protein assay kit as per instructions. Fractions containing the GST-Chk1 were pooled and diluted to a concentration of ~0.5mg/ml and dialyzed for 4 hours at 4^0C in dialysis buffer (20mM HEPES, pH 7.0, 1mM Manganese Acetate, 100mM $NaCl_2$, 0.05% Brij-35, 10% glycerol, 1mM DTT, 0.2% (v/v) protease inhibitor cocktail, 1mM sodium orthovanadate). The protein was aliquoted and stored at -80^0.

Cell Cycle Studies:

Drug studies considering cellular effects were performed in the Hela S3 adherent cell line. Cells were plated at a concentration sufficiently low such that 24 hours later they were at 10-20% confluence (typically $2x10^5$ cells/15cm e3). Cells were then synchronized in S phase by a repeated thymidine block. Briefly, cells were treated with 2mM thymidine for 18hours, released for 8 hours by 3 washes, and then treated again with thymidine. Following the second release from thymidine, 95% of cells were in S phase. Synchronized cells were then returned to complete media containing a DNA-damaging drug such as 50nM topotecan (a dosage we have found to be sufficient to arrest cells in early G2 phase without inducing apoptosis) alone and in combination with test compounds for up to 18 hours. Cell cycle profiles were then performed cytometrically using a procedure for propidium iodide staining of nuclei. (Vindelov et al, Cytometry Vol.3, No.5, 1983, 323-327) CHK1 inhibitors would be expected to reverse the G2 arrest caused by the DNA damaging agent. Typical concentration ranges for such activity would be 0.001 to 10 uM.

Proliferation/Apoptosis Studies:

Proliferation studies were performed in a variety of adherent and non-adherent cell lines including Hela S3, HT29, and Jurkat. The proliferation assay utilized a colorimetric change resulting from reduction of the tetrazolium reagent XTT into a formazan product by metabolically active cells (Scudiero et al. Cancer Research, 48, 1981, 4827-4833) Cells were seeded in 100ul in 96 well plates to roughly 10% confluence (cell concentration varied with cell lines) and grown for 24 hours. Compounds were then added with or without sufficient vehicle- containing media to raise the cells to a 200ul final volume

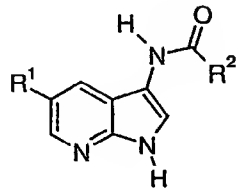
containing chemical reagents in 0.2% DMSO. Cells received multiple concentrations of DNA-damaging anti-proliferative drugs such as topotecan, test compounds, and combination treatment at 37°C 5% CO_2. 72 hours later, 50 uls of an XTT/ phenazine methosulfate mixture were added to each well and cells were left to incubate for 90mins. Plate was read at 450nm, and anti-proliferative effects were compared relative to vehicle treated cells. CHK1 inhibitors are expected to enhance the cytotoxicity of DNA-damaging chemotherapeutic drugs. Typical concentration ranges for such activity would be 0.001 to 10 uM. Other assays for cellular proliferation or cytotoxicity could also be used with test compounds, and these assays are known to those skilled in the art.

Formulations for pharmaceutical use incorporating compounds of the present invention can be prepared in various forms and with numerous excipients. Examples of such formulations are given below:

All publications, including but not limited to patents and patent applications cited in this specification are herein incorporated by reference as if each individual publication were specifically and individually indicated to bc incorporated by reference as though fully set forth.

What is claimed is:

1. A compound according to Formula (I) hereinbelow:



(I)

wherein:

R^1 is aryl or heteroaryl, wherein aryl or heteroaryl may optionally be substituted by one or more of group A and on any position with the exception that R^1 is not 3,4-dichlorophenyl,

A is selected from the group consisting of C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, C_{0-6} alkylheteroaryl, $C(=NH)R^3$, COR^3, $CONR^3R^4$, $CON(O)R^3R^4$, CO_2R^3, $C(O)SR^3$, $C(S)R^3$, cyano, trifluoromethyl, NR^3R^4, $N(O)R^3R^4$, NR^3COR^4, $NR^3CONR^4R^5$, $NR^3CON(O)R^4R^5$, $NR^3CO_2R^3$, $NR^3C(O)SR^3$, $NR^3SO_2R^3$, nitro, OR^3, OCF_3, aryloxy, heteroaryloxy, SR^3, $S(O)R^3$, $S(O)_2R^3$, SCF_3, $S(O)CF_3$, $S(O)_2CF_3$, $SO_2NR^3R^4$, SO_3R^3, $PO_3R^3R^4$, and halo, wherein C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-5} alkylaryl, C_{0-5} alkylheterocyclyl, C_{0-5} alkylheteroaryl, $(CH_2)_{0-5}$heteroaryl, aryloxy, and heteroaryloxy may be optionally substituted by one or more of group B and on any position;

B is selected from the group consisting of C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-5} alkylaryl, C_{0-5} alkylheterocyclyl, C_{0-6} alkylheteroaryl, $C(=NH)R^3$, COR^3, $CONR^3R^4$, $CON(O)R^3R^4$, CO_2R^3, $C(O)SR^3$, $C(S)R^3$, cyano, trifluoromethyl, NR^3R^4, $N(O)R^3R^4$, NR^3COR^4, $NR^3CONR^4R^5$, $NR^3CON(O)R^4R^5$, $NR^3CO_2R^3$, $NR^3C(O)SR^3$, $NR^3SO_2R^3$, nitro, OR^3, OCF_3, aryloxy, heteroaryloxy, SR^3, $S(O)R^3$, $S(O)_2R^3$, SCF_3, $S(O)CF_3$, $S(O)_2CF_3$, $SO_2NR^3R^4$, SO_3R^3, $PO_3R^3R^4$, and halo, wherein C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, C_{0-6} alkylheteroaryl, $(CH_2)_{0-6}$heteroaryl, aryloxy, and

heteroaryloxy may be optionally substituted by one or more of group C and on any position;

R^3, R^4, and R^5 are independently selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, and C_{0-6} alkylheteroaryl; or R^3 and R^4 taken together with the nitrogen to which they are attached form a ring having 3 to 7 carbon atoms optionally containing 1, 2, or 3 heteroatoms selected from nitrogen, sulfur, oxygen, or nitrogen, substituted with hydrogen, C_{1-6} alkyl or $(CH_2)_{0-3}$aryl, wherein any of the foregoing may be optionally substituted by one or more of group C and on any position;

C is selected from the group consisting of C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, C_{0-6} alkylheteroaryl, $C(=NH)R^6$, COR^6, $CONR^6R^7$, $CON(O)R^6R^7$, CO_2R^6, $C(O)SR^6$, $C(S)R^6$, cyano, trifluoromethyl, NR^6R^7, $N(O)R^6R^7$, NR^6COR^6, $NR^6CONR^7R^8$, $NR^6CON(O)R^7R^8$, $NR^6CO_2R^6$, $NR^6C(O)SR^6$, $NR^6SO_2R^6$, nitro, OR^6, OCF_3, aryloxy, heteroaryloxy, SR^6, $S(O)R^6$, $S(O)_2R^6$, SCF_3, $S(O)CF_3$, $S(O)_2CF_3$, $SO_2NR^6R^7$, SO_3R^6, $PO_3R^6R^7$, and halo, wherein C_{1-8} alkyl, C_{1-8} alkanoyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, C_{0-6} alkylheteroaryl may be optionally substituted by one or more of $C(=NH)R^6$, COR^6, $CONR^6R^7$, $CON(O)R^6R^7$, CO_2R^6, $C(O)SR^6$, $C(S)R^6$, cyano, trifluoromethyl, NR^6R^7, $N(O)R^6R^7$, NR^6COR^6, $NR^6CONR^7R^8$, $NR^6CON(O)R^7R^8$, $NR^6CONR^6R^7R^8Y$, $NR^6CO_2R^6$, $NR^6C(O)SR^6$, $NR^6SO_2R^6$, nitro, OR^6, aryloxy, heteroaryloxy, SR^6, $S(O)R^6$, $S(O)_2R^6$, $SO_2NR^6R^7$, SO_3R^6, $PO_3R^6R^7$, or halo, and on any position;

R^6, R^7, and R^8 are independently selected from the group consisting of hydrogen, C_{1-10} alkyl, C_{1-10} alkanoyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkyl, C_{0-6} alkylaryl, C_{0-6} alkylheterocyclyl, and C_{0-6} alkylheteroaryl; or R^7 and R^8 taken together with the nitrogen to which they are attached form a ring having 3 to 7 carbon atoms

optionally containing 1, 2, or 3 heteroatoms selected from nitrogen, sulfur, oxygen, or nitrogen, substituted with hydrogen, C_{1-6} alkyl or $(CH_2)_{0-3}$aryl;

R^2 is selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl, C_{3-6} cycloalkyl, OR^9, $NR^{10}R^{11}$, phenyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazolinyl, thiazinyl, pyrrolyl, furyl, thienyl, pyrazolyl, imidazolyl, triazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl and thiadiazolyl, wherein alkyl and alkenyl and cycloalkyl may optionally be substituted with one of more of group D and at any position and wherein phenyl may be optionally subtituted at positions 3-, 4-, and 5- with one to three of group E and wherein pyridyl, pyridazinyl, pyrimidinyl, pyrazolinyl, thiazinyl, pyrrolyl, furyl, thienyl, pyrazolyl, imidazolyl, triazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl and thiadiazolyl may optionally be substituted by one or more of group F and at any position, with the preferred substitution being *n*-propyl or pyridyl or pyrazolinyl, with the more preferred substitution being 3-pyridyl
R^9 is hydrogen or C_{1-6} alkyl, wherein any of the foregoing groups are optionally substituted with one or more of group D and at any position, with the exception that R^9 is not *tert*-butyl;
R^{10} is selected from the group consisting of hydrogen, methyl and ethyl;
R^{11} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-8} alkenyl and C_{3-6} cycloalkyl, wherein any of the foregoing groups are optionally substituted with one or more of group D and at any position;
R^{10} and R^{11} taken together with the nitrogen to which they are attached may form a ring having 3 to 7 carbon atoms optionally containing 1, 2, or 3 heteroatoms selected from nitrogen, sulfur, oxygen, or nitrogen, substituted with hydrogen or C_{1-6} alkyl;
D is selected from the group consisting of C_{1-6} alkyl, C_{2-8} alkenyl, C_{3-6} cycloalkyl, OR^{12}, $OC(O)NR^{12}R^{13}$, $NR^{14}SO_2R^{12}R^{13}$, $NR^{14}C(O)OR^{12}$, $NR^{14}C(O)NR^{12}R^{13}$, halo, cyano, trifluoromethyl, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, SO_3R^{12}, $SO_2NR^{12}R^{13}$, $C(O)SR^{12}$, $CONR^{12}R^{13}$ and PO_3R^{12};
R^{12}, R^{13}, R^{14} are independently selected from the group consisting of hydrogen, C_{1-3} alkyl, C_{2-3} alkanoyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and C_{3-5} cycloalkyl; or R^{12} and R^{13} taken together with the nitrogen to which they are attached form a ring having 3 to 7

carbon atoms optionally containing 1, 2, or 3 heteroatoms selected from nitrogen, sulfur, oxygen, or nitrogen, substituted with hydrogen or C_{1-3} alkyl;
E is selected from the group consisting of C_{1-4} alkyl, OR^{15} and $NR^{15}R^{16}$, with the exception that R^2 is not 3,4-dimethoxyphenyl or 3-methoxyphenyl,
F is selected from the group consisting of C_{1-6} alkyl, C_{2-8} alkenyl, C_{3-6} cycloalkyl, OR^{12}, $OC(O)NR^{12}R^{13}$, $NR^{12}R^{13}$, $NR^{14}SO_2R^{12}R^{13}$, $NR^{14}C(O)OR^{12}$, $NR^{14}C(O)NR^{12}R^{13}$, halo, cyano, trifluoromethyl, SR^{12}, $S(O)R^{12}$, SO_2R^{12}, SO_3R^{12}, $SO_2NR^{12}R^{13}$, $C(O)SR^{12}$, $CONR^{12}R^{13}$ and PO_3R^{12};
R^{15} and R^{16} are independently selected from the group consisting of hydrogen, C_{1-3} alkyl, C_{2-3} alkanoyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and C_{3-5} cycloalkyl; or R^{15} and R^{16} taken together with the nitrogen to which they are attached form a ring having 3 to 7 carbon atoms optionally containing 1, 2, or 3 heteroatoms selected from nitrogen, sulfur, oxygen, or nitrogen, substituted with hydrogen or C_{1-3} alkyl.

2. A compound according to claim 1 wherein any substitution at R1 is 3-,4- or 5-alkoxy- or hydroxy- or amino- or hydroxymethyl- or aminomethyl- or acetamido- or aminosulfamoyl- or dimethylamino- phenyl including di- and tri-substitution or 3-thienyl.

3. A compound according to claim 2 wherein any substitution at R1 is 4-hydroxy-3-methoxyphenyl or 3-acetamidophenyl or 3,4-dimethoxyphenyl or 4-aminophenyl or 4-aminomethylphenyl;

4. A compound according to claim 1 wherein the compound is selected from the group consisting of:
3-dimethylamino-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;
4-methoxy-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;
1-ethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-urea;
benzo[1,3]dioxole-5-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;
N-(5-(3-carboxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-chloro-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

N-(5-(4-carboxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

4-acetylamino-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

N-(5-(3-chloro-phenyl)-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-isonicotinamide;

acetic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-ylcarbamoyl)-methyl ester;

6-(2-(pyrrolidin-1-yl)ethyl-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

3-hydroxy-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;

N-(5-(4-cyano-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-acetyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(pyridin-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-fluoro-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-methyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-carbamic acid ethyl ester;

N-(5-(4-methylsulfonyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

2-methoxy-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-acetamide;

(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-hydroxymethyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

pyridine-2-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

N-(5-(pyridin-4-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-isobutyramide;

N-(5-(4-dimethylamino-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-hydroxymethyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

6-methyl-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

thiophene-2-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

N-(5-(4-sulfamoylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-aminophenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-acetamido-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-hydroxy -phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

furan-2-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

furan-3-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

thiophene-3-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

pyrrole-2-carboxylic acid (5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide

N-(5-(4-methyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-(morpholin-1-yl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-(4-methyl-piperazin-1-yl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

5-methyl-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

5-bromo-*N*-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

2,6-dimethoxy-*N*-(5-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-aminomethylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-formylphenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-(4-t-butoxycarbonyl)-piperazinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(4-(4-t-butoxycarbonyl)-piperazinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-(4-t-butoxycarbonyl)-methyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

N-(5-(3-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(3-(4-methylpiperazinomethyl)-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;

N-(5-(4-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;
N-(5-(4-(4-methylpiperazinomethyl)-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;
2-methyl-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;
2-chloro-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;
N-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-2-methoxybenzamide;
2-hydroxy-*N*-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-benzamide;
pyrimidine-5-carboxylic acid-((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;
N-((5-(benzothiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-((5-(thiophen-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-((5-(3-biphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-((5-(benzofuran-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-((5-(indol-5-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
pyrazine-2-carboxylic acid ((5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide; and
N-(5-(4-aminomethylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide.

5. A compound according to claim 4 selected from the group consisting of :
N-(5-(thiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;
N-(5-(4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;
N-(5-(3,4-dimethoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;
N-(5-(3-sulfamoylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;
N-(5-(3-acetamide-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;
N-(5-(naphthalen-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
4-methyl-*N*-(5-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
pyrazine-2-carboxylic acid (5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-amide;

N-(5-(4-aminomethylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-butyramide;
N-(5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-methoxyphenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-dimethylamino-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3,4-(methylenedioxy)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3,5-dimethyl-4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-hydroxymethyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(thiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-aminophenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3,4-dimethoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3-acetamido-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-(dimethylaminomethyl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3,5-dimethyl-4-hydroxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-hydroxymethyl-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-diethanolaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3-dimethylaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3-(4-methylpiperazinomethyl)-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3-diethanolaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-(morpholin-1-yl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide; and
N-(5-(4-(4-methyl-piperazin-1-yl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide.

6. A compound according to claim 5 selected from the group consisting of :
N-(5-(4-morpholinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-piperidinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;

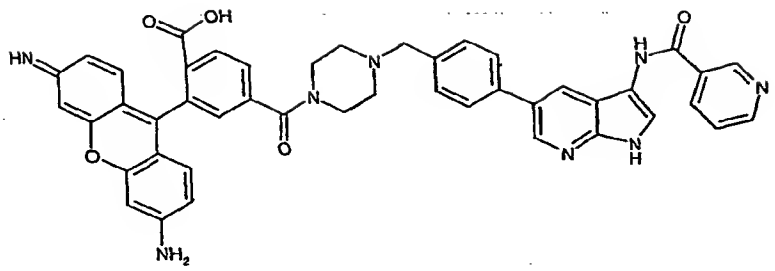
N-(5-(4-pyrrolidinomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-methylaminomethyl-phenyl-1H-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(thiophen-3-yl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-aminophenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3,4-dimethoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(3-acetamido-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-hydroxy-3-methoxy-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-(dimethylaminomethyl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide;
N-(5-(4-(morpholin-1-yl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide; and
N-(5-(4-(4-methyl-piperazin-1-yl)-phenyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-nicotinamide.

7. A method of inhibiting angiogenesis or damage response kinase activity which comprises administering to a subject in need thereof, an effective amount of a compound according to claim 1.

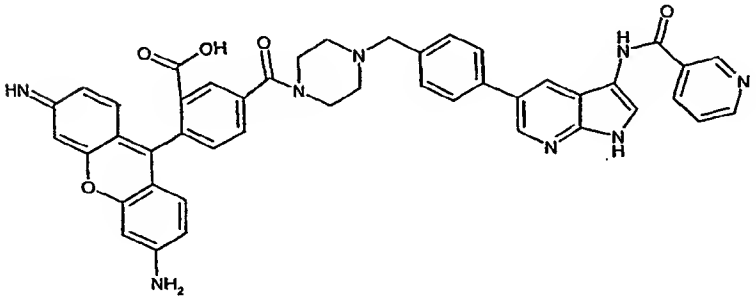
8. A method according to claim 7 wherein the kinase being inhibited in chk-1 kinase.

9. A method according to claim 7 wherein the disease or disorder being treated is selected from the group consisting of leukemia, solid tumor cancer, metastases, lymphomas, soft tissue cancers, brain cancer, esophageal cancer, stomach cancer, pancreatic cancer, liver cancer, lung cancer, bladder cancer, bone cancer, prostate cancer, ovarian cancer, cervical cancer, uterine cancer, testicular cancer, kidney cancer, head cancer and neck cancer, chronic inflammatory proliferative diseases, proliferative cardiovascular diseases, proliferative ocular disorders and benign hyperproliferative diseases.

10. A compound with the formula below:



and



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/31842

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/437, 31/496, 31/497, 31/506, 31/5377; A61P 35/00; C07D 471/04, 405/14, 403/14, 413/14
US CL : 514/300, 234.5, 253.04, 255.05, 256; 544/127, 233, 362, 405; 546/113

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 514/300, 234.5, 253.04, 255.05, 256; 544/127, 233, 362, 405; 546/113

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,750,536 A (MANTOVANINI et al) 12 May 1998 (12.05.1998), column 1.	1-10
A	US 5,681,959 A (BISHOP et al) 28 October 1997 (28.10.1997), column 2; column 7, Example 10.	1-10
A	DE 100 53 122 A1 (ROSSELL et al) 23 May 2001 (23.05.2001), page 2.	1-10
A	JACKSON et al. An indolocarbazole inhibitor of human checkpoint kinase (Chk1) abrogates cell cycle arrest caused by DNA damage. Cancer Research. 01 February 2000, Vol. 60, No. 3, pages 566-572, especially page 566.	1-10

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
22 November 2002 (22.11.2002)

Date of mailing of the international search report
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INTERNATIONAL SEARCH REPORT

PCT/US02/31842

Continuation of B. FIELDS SEARCHED Item 3:
CAS ONLINE
MEDLINE search terms: checkpoint kinase, inhibitor, inhibit